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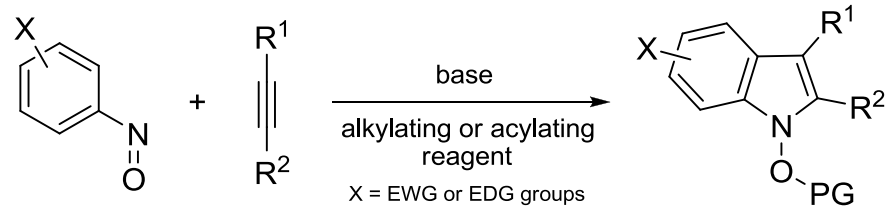
UNIVERSITÀ DEGLI STUDI DI TORINO

GRAPHICAL ABSTRACT



A simple, efficient, regioselective and one-pot preparation of *N*-hydroxy- and *N*-*O*-protected hydroxyindoles via cycloaddition of nitrosoarenes with alkynes. Synthetic scope, applications and novel by-products.

Gabriella Ieronimo[a], Alessandro Mondelli[a], Francesco Tibiletti[a], Angelo Maspero[a], Giovanni Palmisano[a], Simona Galli[a], Stefano Tollari[a], Norberto Masciocchi[a], Kenneth M. Nicholas[b], Silvia Tagliapietra[c], Giancarlo Cravotto[c], Andrea Penoni*[a]

a) Dipartimento di Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, via Valleggio 11, 22100 Como - Italy
b) Department of Chemistry and Biochemistry, University of Oklahoma, Stephenson Life Sciences Research Center, 101 Stephenson Parkway, Norman, OK 73019-5251
c) Dipartimento di Scienza e Tecnologia del Farmaco, Università degli Studi di Torino, Via P. Giuria 9, 10235 Torino, Italy

*corresponding author:
Phone +39-031-2386440; Fax +39-031-2386449; E-mail: andrea.penoni@uninsubria.it

ABSTRACT

The thermal reaction between nitrosoarenes and alkynes under alkylating conditions produces *N*-alkoxyindoles as the major products in moderate to good yields and excellent regioselectivity. Various electrophiles are used affording different *N*-*O*-protected hydroxyindoles in a multi-component fashion. Privileged acetylenic subtrates used in reactions with substituted nitrosoarenes are arylalkynes or propiolates. Potentially bioactive compounds and other classes of highly functionalizable indole products were prepared. Reactions between *o*-carbomethoxy-nitrosoarenes and arylacetylenes provided tricyclic compounds containing an acylaziridine indoline skeleton.

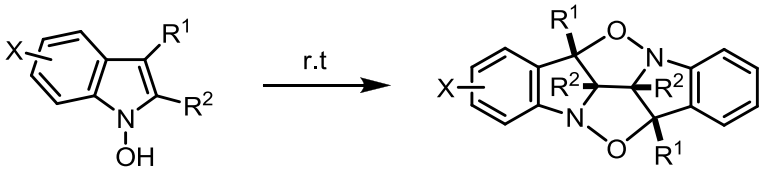
KEYWORDS: *Nitrosoarenes, Alkynes, Indoles, Annulation, N-Heterocycles*

INTRODUCTION

Indoles are among the most interesting and well-known heterocycles. Their structure is particularly valuable in medicinal chemistry, chemical biology and pharmaceutical sciences since the indole ring is so prevalent in molecules that show biological activities and. Many methods have been reported for the preparation of the indole skeleton.[1] Rarer *N*-hydroxy- and *N*-alkoxyindoles were studied by different research groups both in academic and industrial laboratories for their potential significance as novel reactive compounds, useful synthetic intermediates and bioactive natural products.[2] The provocative "1-hydroxyindole hypothesis" was introduced by Somei[3] to support the biological role of 1-hydroxyindoles in the biosynthesis and functionalization of indole alkaloids and inside some biological pathways. The search for new drugs has shown in recent years that *N*-hydroxyindole and *N*-alkoxyindole derivatives and their related compounds were studied for their potential activity in reducing the risk of cancer.[4] The 1-Hydroxyindole nucleus was recently discussed in pigments from flower pot parasol *Leucocoprinus birnbaumii*[5] a specie of a gilled mushroom in the family of Agaricaceae.[5] Among naturally occurring compounds with *N*-methoxyindole skeletons, paniculidine B an alkaloid isolated from *Murraya paniculata* and phytoalexin analogues of Wasabi (*Wasabia japonica* a plant member of the family of the Brassicaceae) were found.[6] In the last decade it was observed that some indole-based pharmaceutical agents were improved after replacing the N-H with an *N*-alkoxy moiety.[7]

Although some methods to produce *N*-alkoxy- and *N*-hydroxyindoles and other complex structures containing the *N*-hydroxyindole unit have been published,[8] their utility has been limited by low yields and competing reactions. The most established synthetic route to these compounds is Somei's method, which starts from a preformed indole *via* reduction to the indoline, followed by the tungstate-catalyzed reoxidation to the *N*-hydroxyindole.[2b] More recently, Nicolaou and Wojciechowski reported a new synthetic pathway to produce *N*-hydroxyindoles by Sn(II)-induced reductive cyclizations of *o*-nitrounsaturated ketoesters and this technique was efficiently used in the preparation and construction of nocathiacin I model systems.[9] Baran and Myers independently reported the total synthesis of dimeric stephacidin B and of the corresponding monomer avrainvillamide.[10] As reported by Chang, Zhao and coauthors not many methods are known to produce the *N*-alkoxyindole skeleton directly.[11] Besides other less efficient or less general methods, an efficient Pb-promoted reductive cyclization of *o*-nitrobenzyl ketones to *N*-hydroxyindoles has been recently described.[12]

The stability of *N*-hydroxyindoles has been discussed in many reports and was a focus of debate.[2b,13] Some *N*-hydroxyindoles are elusive and highly unstable compounds and easily convert to dehydrodimerization products, known as 1,10-diaza-9,20-dioxakabutane named after an ancient helmet of the Japanese Army[2b, 14] (Scheme 1). The first isolation and characterization of this class of compounds was performed by Tedder in the sixties[15] and later confirmed by X-ray diffraction.[16]



Scheme 1. Dehydrodimerization of *N*-hydroxyindoles to kabutanes

The elusive and labile nature of *N*-hydroxyindoles led to the introduction of some techniques to produce the more stable *N*-methoxy- and *N*-alkoxyindoles.[17] *N*-Alkoxy-derivatization of indole-3-carbinol was recently reported to increase the efficacy of G cell cycle arrest and it was detected to be active in the regulation of cell cycle gene transcription and activity in time guest cancer cells.[18] Most of the synthetic protocols to access the *N*-alkoxyindole unit come from intramolecular reactions.[19] A noteworthy and remarkable synthetic approach to the formation of *N*-alkoxyindole framework is the heterocyclization reported by Zhao and coworkers on 3-alkoxyimine-2-arylalkylnitriles mediated by ferric chloride.[11] It is known that 2-nitrostyrenes and 2-nitrostilbenes react in under reducing conditions giving the selective formation of indoles.[20] A theoretical study by Davies and Houk provided evidence that in the deoxygenation of nitroaromatics for the construction of nitrogen containing heterocycles an alternative pathway through a 6π-electron 5-atom electrocyclization of nitrostyrenes, nitrostilbenes and nitrobiphenyls can give nitronate intermediates that rapidly evolve to *N*-hydroxy heterocycles.[21]

Our group continues to show a strong interest in organic and organometalic chemistry of indole derivatives.[22] Previous experience in this research topic led some of us to introduce an intramolecular synthesis of 2-substituted *N*-hydroxyindoles starting from 2-nitrostilbenes by using $Pd(TMB)_2$ (TMB = trimethylbenzoate) as catalyst under CO.[23] Very recent contributions by Peet and coworkers[24] on the study of the mechanism of the Cadogan-Sundberg indole synthesis and on the preparation of phytoalexin from Wasabi revealed the formation of *N*-hydroxyindoles as major products by reduction of nitrostilbenes with triethyl phosphite under microwave irradiation[24a] and trimethyl phosphite.[24b] From our ongoing studies on the activation/nitrogenation of unfunctionalized hydrocarbons we also disclosed a new synthetic, regioselective

and versatile intermolecular approach to indoles using nitro compounds as precursors (Figure1). The reductive annulation of nitroarenes with alkynes under CO with Cp-iron and -ruthenium complexes as catalysts furnished 3-substituted indoles regioselectively.[25] Ragaini and co-workers optimized this reaction using Pd[26a]- and mixed Pd-Ru catalysts.[26b] A preliminary and explorative study of the reaction of arynes with nitrosobenzene was originally reported by Steinhoff and Henry.[27a] By this way carbazoles were synthesized as major products. Very recently this reaction was deeply investigated by Studer and co-workers.[27b] Using nitrosoarenes as starting materials we developed an uncatalyzed version of the alkyne cycloaddition that produces *N*-hydroxyindoles as the major products more rapidly and in higher yields (Figure 1).[28] The efficiency of the ArNO/alkyne cycloaddition can be improved significantly by alkylative trapping of the labile *N*-hydroxyindoles with K_2CO_3-Me_2SO_4 isolating *N*-methoxyindoles as the major products (Figure 1).[29] This method was used to achieve in good yields and few synthetic steps a phytoalexin derived analogue of Wasabi. The mechanism of the reaction was studied using kinetic experimental probes and computational methods revealing the likelihood of a stepwise radical pathway with the formation of the carbon-nitrogen bond as the rate determining step.[30] More recently the nitrosoarene-alkyne cycloaddition was introduced as a new synthetic approach to the meridianin natural products, marine indole alkaloids established as kinase inhibitors.[31] Some of us reported an indole synthesis starting from arylhydroxylamines via the intermediate formation of nitrosoaromatics.[32] Very recently Srivastava and coworkers implemented the indolization by annulations of nitrosoarenes with alkynes adding gold[33a] and copper[33b] catalysts to obtain indoles in one-pot procedure in the presence of reducing agents.

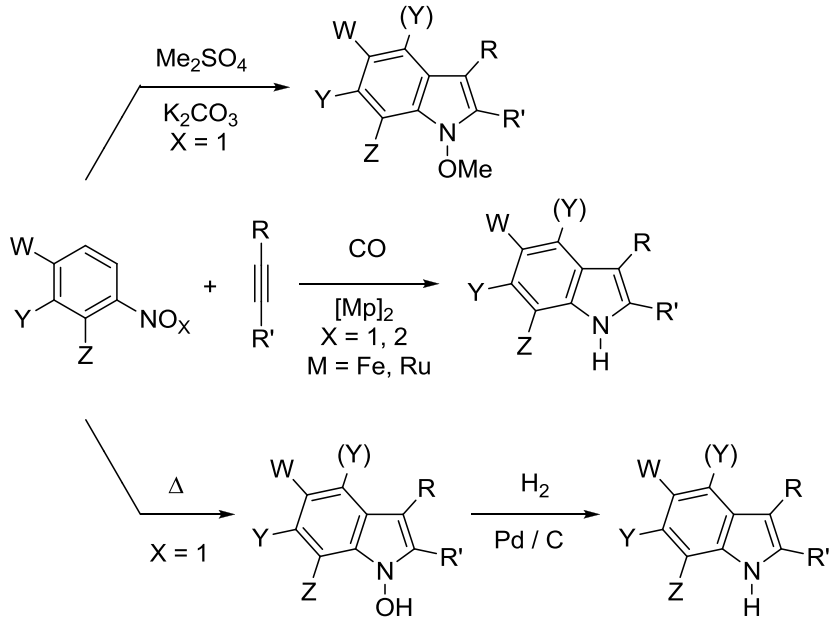
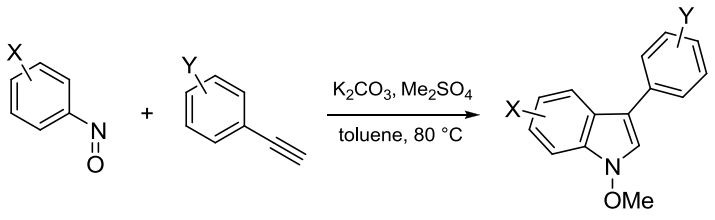


Figure 1. Synthesis of indole compounds by cycloaddition of nitro- and nitrosoaromatics with alkynes

RESULTS AND DISCUSSION

In this paper an extended and detailed survey of the preparation of *N*-alkoxyindoles and other *O*-protected 1-hydroxyindoles using different electrophiles (alkylating and acylating reactants) in a one-pot procedure by annulation of nitrosoarenes with alkynes is presented. In the aim to show the general purpose of the reaction, the synthetic application and the substrate scope, other terminal and internal alkynes were used and tested in a wide survey with both electron-rich and electron-deficient nitrosoaromatics. The scope of the present study is the general application of the synthetic protocol for the preparation of *N*-*O*-protected hydroxyindoles using a variety of arylalkynes or propiolates and a wide range of electrophiles. As already seen, to avoid the

side reaction of the formation of kabutanes, we organized a multi-component procedure to protect *N*-hydroxyindoles as the corresponding *N*-methoxy derivatives.[29] Multicomponent reactions (MCRs) are frequently and deeply studied and known as convergent reactions, in which three or more starting materials react in a sequential manner to form prevalently a single product, where basically all or most of the atoms are incorporated into the newly formed product in a highly selective way.[34] Different protecting groups were used showing the potential to afford various indole protected compounds maintaining the regioselectivity both with arylacetylenes and propiolates. *N*-Alkoxyindoles are produced in moderate to excellent yields from the reaction between substituted-nitrosoarenes and substituted-arylacetylenes under alkylative conditions, in the presence of K_2CO_3/Me_2SO_4. Generally, nitrosoarenes with electron withdrawing groups react faster than electron-rich nitrosoaromatics and show better yields and selectivities for the indole products. Nitrosoarenes are usually used as the limiting reagents and with most of the reactions being carried out with an excess of the alkyne. Conjugated alkynes were found to be the privileged partners for the cyclization and reactions carried out with unconjugated alkynes and symmetrical internal alkynes (diphenylacetylene, bis-trimethylsilylacetylene and 4-octyne) gave poor yields or no reactions at all. Terminal alkynes show better yields of the indole compounds than internal alkynes and all the reactions show exclusively the formation of 3-substituted indoles without any traces of the other regioisomer. Nitrosoarenes **1a-f** reacted in the presence of an excess (12 fold) of the arylacetylenes **2a-i** using K_2CO_3 as base and Me_2SO_4 as the methylating agent (6:1 molar ratio relative to the nitrosoarene). Products **3a-q** were achieved in 4-12 h in good to excellent yields (Scheme 2 and Table 1)



1 a-f **2 a-i** **3 a-q**

1a: X = 4-NO_2
1b: X = 4-CN
1c: X = 4-Br
1d: X = 2,5-COOMe
1e: X = H
1f: X = 4-OMe

2a: Y = 4-NO_2
2b: Y = 4-CN
2c: Y = 4-Br
2d: Y = 4-Cl
2e: Y = 2-NHCOMe
2f: Y = 4-NHCOMe
2g: Y = H
2h: Y = 4-Me
2i: Y = 4-OMe

3a: X = 5-NO_2, Y = 4-NO_2; **3b: X = 5-NO_2, Y = 4-CN**
3c: X = 5-NO_2, Y = 4-Br; **3d: X = 5-NO_2, Y = 4-Cl**
3e: X = 5-NO_2, Y = 2-NHCOMe; **3f: X = 5-NO_2, Y = 4-NHCOMe**
3g: X = 5-NO_2, Y = 4-Me; **3h: X = 5-NO_2, Y = 4-OMe**
3i: X = 5-CN, Y = H; **3j: X = 5-Br, Y = H**
3k: X = 4,7-COOMe, Y = H; **3l: X = H, Y = 4-NO_2**
3m: X = H, Y = 4-CN; **3n: X = H, Y = 4-Cl**
3o: X = H, Y = 4-Me; **3p: X = H, Y = 4-OMe**
3q: X = 5-OMe, Y = H

Scheme 2. Synthesis of 3-aryl-substituted *N*-Methoxyindoles

The electronic properties of the Y group on the arylacetylenes do not have a dramatic effect on the efficiency of the reaction, although kinetic studies provide some evidence that electron donating groups were found to accelerate the cyclization.[30]

Table 1

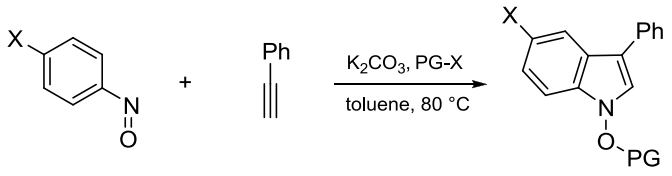
Reactions between nitrosoarenes and arylacetylenes with Me_2SO_4 as the alkylating agent[a]

Entry	Product	X	Y	Yield (%)[b]
1	**3a**	4-NO_2	4-NO_2	91
2	**3b**	4-NO_2	4-CN	82
3	**3c**	4-NO_2	4-Br	77
4	**3d**	4-NO_2	4-Cl	67
5	**3e**	4-NO_2	2-NHCOMe	37
6	**3f**	4-NO_2	4-NHCOMe	55
7	**3g**	4-NO_2	4-Me	48
8	**3h**	4-NO_2	4-OMe	76
9	**3i**	4-CN	H	57
10	**3j**	4-Br	H	47
11	**3k**	2,5-CO_2Me	H	62
12	**3l**	H	4-NO_2	41
13	**3m**	H	4-CN	39
14	**3n**	H	4-Cl	29
15	**3o**	H	4-Me	46
16	**3p**	H	4-OMe	35
17	**3q**	4-OMe	H	25

[a] All reactions were carried out for 4‑12 h using ArNO (1 mmol) and ArC≡CH (12 mmol) with 6 eq of K_2CO_3 and 6 eq. of Me_2SO_4 in 50 ml of toluene at 80 °C under nitrogen

[b] Isolated yields after chromatography

This synthetic route to indoles shows the formation of new C-N and C-C bonds through the activation of an aromatic C-H bond. To possibly extend the substrate scope and for mechanistic purposes pentafluoronitrosobenzene (C_6F_5NO) was studied in a standard reaction with phenylacetylene heating at 80 °C in toluene. After 16 h only starting materials were recovered.



1 a-b **2 g** **4 a-h**

1a: X = NO_2
1b: X = CN

PG-X = Boc_2O
PG-X = $PhCH_2Br$
PG-X = $ClCO_2Et$
PG-X = CbzCl
PG-X = CH_2=$CHCH_2Br$
PG-X = TsCl
PG-X = PhCOCl

4a: X = NO_2; PG = Boc
4b: X = NO_2; PG = $PhCH_2$
4c: X = NO_2; PG = CO_2Et
4d: X = NO_2; PG = Cbz
4e: X = NO_2; PG= CH_2=$CHCH_2$
4f: X = NO_2; PG = Ts
4g: X = CN; PG = CH_2=$CHCH_2$
4h: X = CN; PG = PhCO

Scheme 3. Synthesis of 3-phenyl-substituted *N*-*O*-protected indoles

Several electrophiles (PG-X) reacted efficiently with the intermediate *N*-hydroxyindoles trapping them and giving the final products **4a-h**. The most reactive nitrosoarenes with EWG in *para* position were used with the aim to generalize the multi-component synthetic approach to *N*-*O*-protected hydroxyindoles **4a-h**. Different protecting groups were found to be compatible with the basic reaction conditions. All the

compounds were afforded in good yields by using the base and the alkylating/acylating agent in a 6-fold excess (Scheme 3 and Table 2).

Table 2

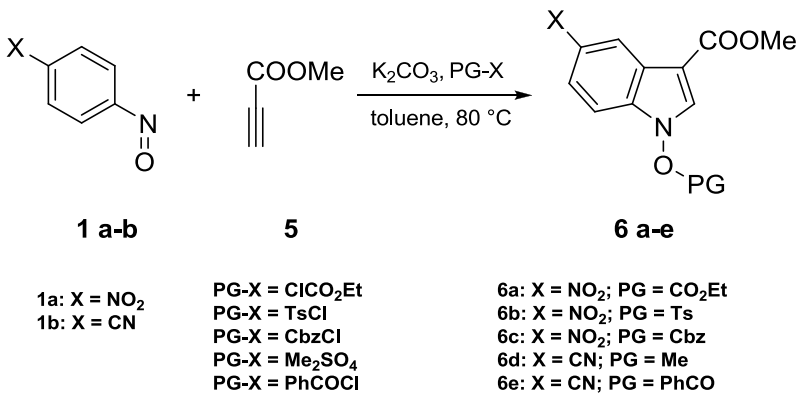
Reactions between nitrosoarenes and phenylacetylene in the presence of different electrophiles[a]

Entry	Product	X	PG-X	Yield (%)[b]
1	**4a**	4-NO_2	Boc_2O	65
2	**4b**	4-NO_2	$PhCH_2Br$	77
3	**4c**	4-NO_2	$ClCO_2Et$	61
4	**4d**	4-NO_2	Cbz-Cl	53
5	**4e**	4-NO_2	CH_2=CH-CH_2Br	86
6	**4f**	4-NO_2	TsCl	32
7	**4g**	4-CN	CH_2=CH-CH_2Br	44
8	**4h**	4-CN	PhCOCl	38

[a] All reactions were carried out for 5‑8 h using ArNO (1 mmol) and PhC≡CH (12 mmol) with 6 eq of K_2CO_3 and 6 eq. of PG-X in 50 ml of toluene at 80 °C under nitrogen

[b] Isolated yields after chromatography

Using propiolates as the acetylenic component in reactions with different nitrosoarenes the same regioselectivity was observed with formation of *N*-*O*-protected-hydroxy-3-carboxyindoles being formed exclusively. In this way a phytoalexin analogue from Wasabi was previously prepared in few steps in good overall yield,[29] introducing an interesting shortcut to this target molecule. The base-promoted multi-component reactions between methyl propiolate, different electrophiles, and various nitrosoarenes also led us to produce indole compounds **6a-e** in good yields (Scheme 4 and Table 3).



Scheme 4. Synthesis of 3-carbomethoxy-substituted *N*-*O*-protected indoles

Table 3

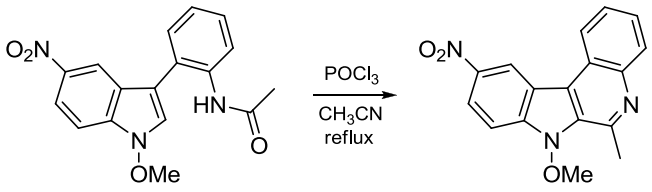
The reactions between nitrosoarenes and methyl propiolate in the presence of different electrophiles[a]

Entry	Product	X	PG-X	Yield (%)[b]
1	**6a**	4-NO_2	$ClCO_2Et$	73
2	**6b**	4-NO_2	TsCl	57
3	**6c**	4-NO_2	CbzCl	60
4	**6d**	4-CN	Me_2SO_4	43
5	**6e**	4-CN	PhCOCl	56

[a] All reactions were carried out for 5‑8 h using ArNO (1 mmol) and PhC≡CH (12 mmol) with 6 eq of K_2CO_3 and 6 eq. of PG-X in 50 ml of toluene at 80 °C under nitrogen

[b] Isolated yields by chromatography

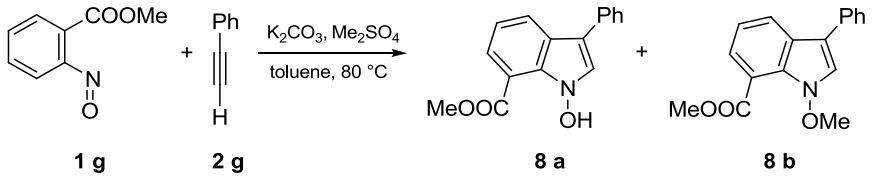
β-Carboline alkaloids, widespread in plants and animals, have been extensively studied and are well known for their biological activity as monoamine oxidase inhibitors (MAOI).[35] Some β-carbolines, notably tryptoline and pinoline, are formed naturally in the human body. The latter is implicated along with melatonin in the role of the pineal gland in regulating the sleep-wake cycle.[36] We envisioned the opportunity to prepare *N*-methoxy-β-carbolines by ring closure through a Bischler-Napieralski type reaction. Thus, treatment of the indole derivative **3e** with $POCl_3$ gave the target molecule **7** in 91% yield (Scheme 5) (overall yield from **1a** = 34%).



3 e **7**

Scheme 5. Synthesis of a representative β-carboline (**7**)

The serendipitous formation of polycyclic derivatives via the intermediate formation of an indoline nitrone was also detected and studied further. The reaction passes through the cyclization of the nitrone via a 1,3-dipolar cycloaddition affording an unstable isoxazoline derivative that is converted to the acylaziridine product. During our survey of the nitrosoarene/alkyne annulation reactions we isolated an unexpected tricyclic byproduct from the reaction between phenylacetylene and *o*-carbomethoxy nitrosobenzene (**1g**) that shed some light on the mechanism of the cycloaddition. This polycyclic compound was detected, isolated and characterized by X-ray diffraction as the major product.[28] The reaction was first carried out under standard alkylating conditions and afforded the *N*-hydroxyindole **8a** in 64% yield with only traces of the corresponding *N*-methoxyindole **8b** (Scheme 6). The alkylation may be inhibited by the formation of a hydrogen bond between the N-OH group and the carbonyl of the ester group in position 7. In contrast to previous experiments, repeating the reaction without an alkylating agent for a longer reaction time. Compound **9f** was produced as the major isolated product, (57%), whose NMR and mass spectra indicated the incorporation of two phenylacetylene units and one nitrosoarene moiety.



1 g **2 g** **8 a** **8 b**

Scheme 6. Reaction between *o*-carbomethoxy-nitrosobenzene and phenylacetylene

The phenylacetylene units in **9** are incorporated in a tail-to-tail fashion C-2, C-2, (Scheme 8) and the carbomethoxy group has migrated from the aromatic carbon to C-1 of an alkyne unit. Although the tricyclic structure of **9** was surprising, a literature search into the skeleton revealed other examples and suggested a pathway for its formation. Analogs of **9** have been obtained from the reactions of indoline nitrones with alkynes, which proceed via dipolar cycloaddition followed by electrocyclic rearrangement of the intermediate isoxazole. A recent substrate survey of *o*-carbomethoxy-nitrosobenzene and 2,5-dicarbomethoxy-nitrosobenzene with different arylacetylenes (Scheme 7 and Table 4) led us to obtain an isoxazoline intermediate derivative that is rapidly converted to acylaziridine product as described by Döpp and other groups.[37] The structure of **9f** was definitely established by X-ray diffraction (Fig. 2) and possesses a 6,5,3-tricyclic skeleton with an aziridine ring fused to a indoline core. An alternative procedure to give compounds with acylaziridine indoline skeleton was reported by Molina and coworkers by reaction of *o*-allylarylazides that generate a nitrene intermediate via loss of dinitrogen.[38] The formation of **9** from the reaction between *ortho*-carbomethoxy nitrosobenzene and phenylacetylene, therefore, suggests the intermediacy of a nitrone (Scheme 8). The intermediacy of an indoline nitrone is implicated from the reaction with *o*-carbomethoxy-nitrosobenzene and arylacetylenes affording tricyclic compounds, likely derived from trapping of a indoline nitrone with a second molecule of arylacetylene to generate an oxazoline that subsequently rearranges to afford acylaziridine indolines.

This species, in turn, may be derived from migratory rearrangement of a non-aromatic precursor such as diradical **A** or nitrone **E**. Working with a dicarbomethoxy substituted nitrosoarene it was possible to isolate both of the diastereoisomers with the aziridineindoline skeleton ring. The two diastereoisomers were characterized and distinguished by coupling constants of the protons on the aziridine ring in ^{1}H-NMR (J^3_{cis} = 7.0 Hz and J^3_{trans} = 5.2 Hz) (Scheme 7). One of these two diastereoisomers, **9f**, was characterized by X-ray diffraction and the structure is shown in Figure 2.

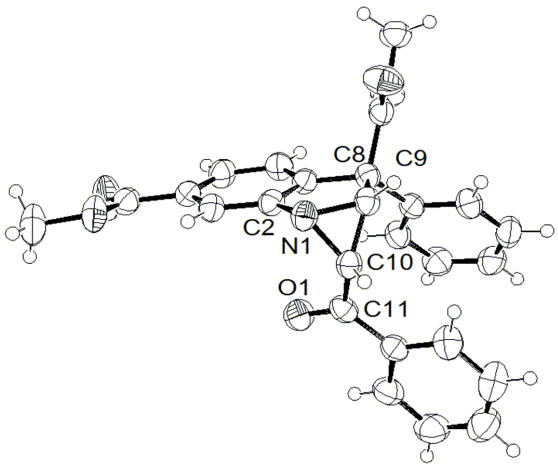
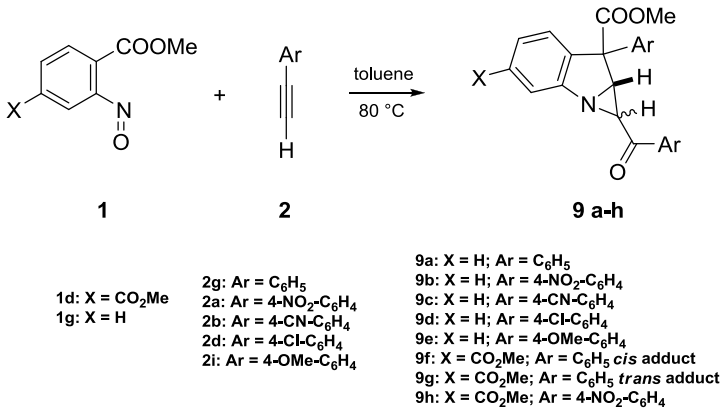


Figure 2. ORTEP drawing of **9f**, with partial labeling scheme. Thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms were given arbitrary radii. Selected bond distances (Å) and angles (°): N1-C2 1.439(2), N1-C9 1.491(2), N1-C10 1.491(2), C8-C9 1.537(3), C10-C11 1.506(3), C11-O1 1.211(2), C2-N1-C9 103.8(2), C2-N1-C10 113.8(2), C9-N1-C10 59.8(1).



Scheme 7. Reactions between *o*-carbomethoxy- and 2,5-dicarbomethoxynitrosoarene and arylacetylenes

Table 4

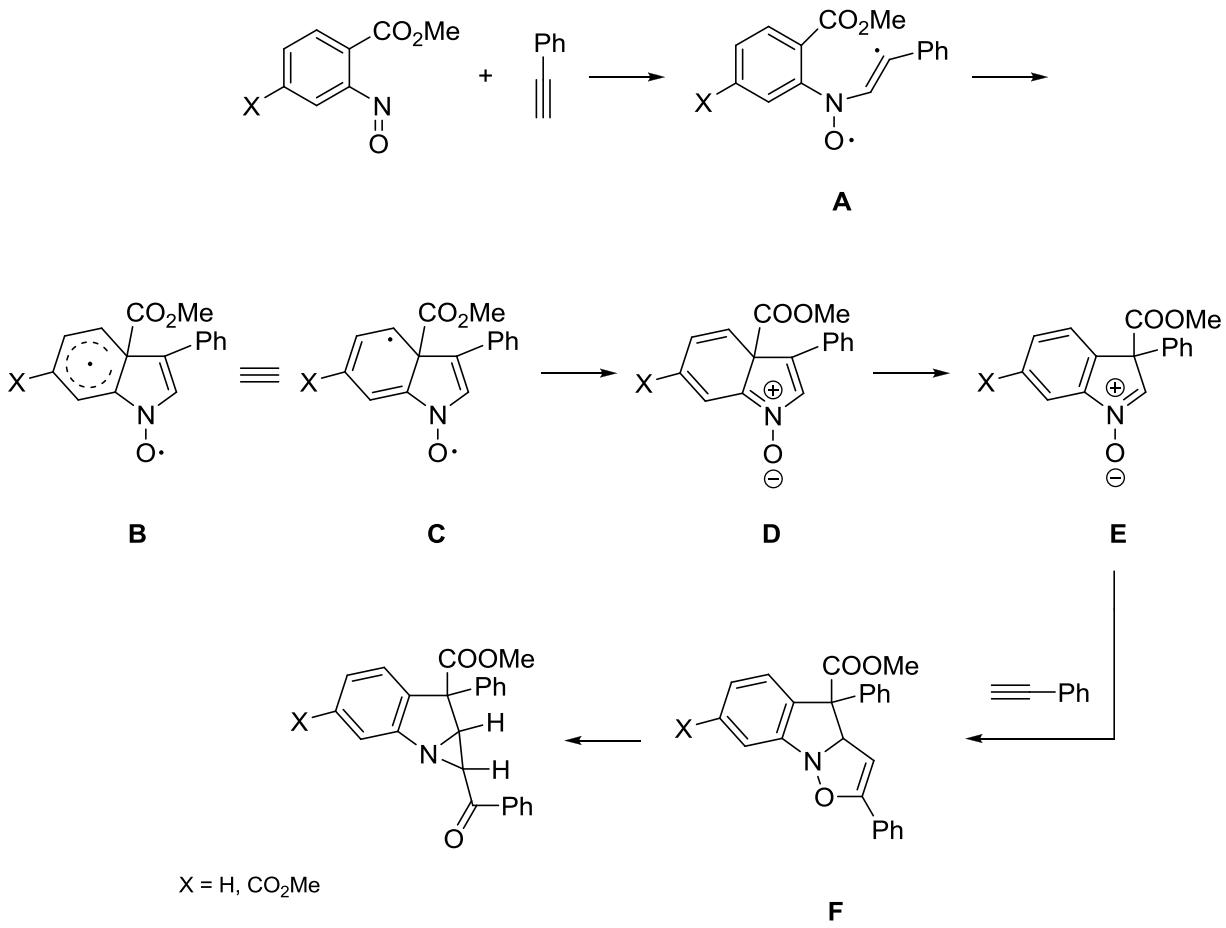
Reactions between *o*-carbomethoxy- and 2,5-dicarbomethoxy-nitrosobenzene with different arylacetylenes[a]

Entry	Product	X	Ar	Yield (%)[b]
1	**9a**	H	C_6H_5	57
2	**9b**	H	4-NO_2-C_6H_4	60
3	**9c**	H	4-CN-C_6H_4	48
4	**9d**	H	4-Cl-C_6H_4	56
5	**9e**	H	4-MeO-C_6H_4	64
6	**9f** + **9g**	CO_2Me	C_6H_5	52 (59/41 *cis*/*trans*)
7	**9h**	CO_2Me	4-NO_2-C_6H_4	44

[a] All reactions were carried out for 4‑8 h using ArNO (1 mmol) and PhC≡CH (12 mmol) in 50 ml of toluene at 80 °C under nitrogen

[b] Isolated yields after chromatography

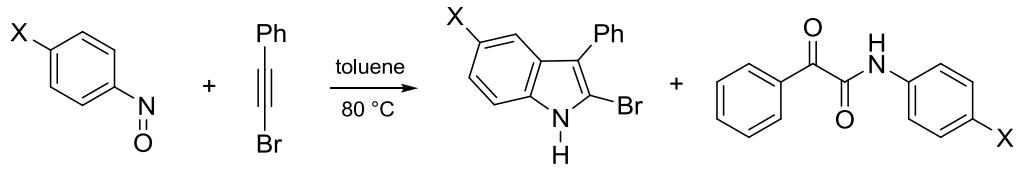
As already stated, computational methods together with kinetic experiments led us to propose a mechanism that shows the intermediacy formation of a radical species that rapidly converts to an indoline nitrone (Scheme 8)[30]



Scheme 8. Proposed mechanism for the formation of compounds **9**

This last reaction works only when using *ortho*-carbomethoxy-nitrosoarene with many different arylalkynes. Examination of the reaction by ^{1}H-NMR showed that the five-membered pyrrole ring temporarily loses aromaticity, as evidenced by the shift of the CO_2Me group.

To expand the substrate scope we studied this indolization procedure with new substrates like 1-bromo-2-phenylacetylene[39] and *p*-tosylacetylene. Three nitrosoarenes with different electronic properties, 4-nitronitrosobenzene, nitrosobenzene and 4-methoxynitrosobenzene, were selected for reaction with 1-bromo-2-phenylacetylene. 2-Bromo-3-phenylindole derivatives, **11a** (45%) and **11b** (51%) were obtained as the major products from 4-nitronitrosobenzene and nitrosobenzene respectively. The product **11a** was fully characterized and the X-ray diffraction structure is given in Figure 3. Unusual side products **12b** and **12c** with a α-ketoamide fragment were isolated from the reactions between 1-bromo-2-phenylacetylene and nitrosobenzene and 4-methoxynitrosobenzene (Scheme 9). With *p*-methoxy-nitrosobenzene the chemoselective formation of the α-ketoamide product **12c** in 62% yield occurs without any trace of indole product **11c**. The reactions leading to products **12b** and **12c** will be studied further to gain mechanistic insights into their mode of formation. In a previous report by Jiao the same α-ketoamide compounds and analogues were prepared by copper-catalyzed oxidative amidation-diketonization of terminal alkynes.[40] Conversely, no traces of **12a** were detected in the reaction between 4-nitronitrosbenzene and 1-bromo-2-phenylacetylene.



1 **10** **11** **12**

1a: X = NO_2
1e: X = H
1f: X = OMe

11a: X = NO_2
11b: X = H
11c: X = OMe

12a: X = NO_2
12b: X = H
12c: X = OMe

Scheme 9. Reactions between *p*-substituted nitrosoarenes and 1-bromo-2-phenylacetylene

The electronic properties of the substituent on the nitrosoaromatic seem to play a dramatic role driving the reaction to the formation of the indole compound or to the α-ketoamide product. 2-Bromoindoles are interesting scaffolds that can be further functionalized by Suzuki-Miyaura type reaction with boronic acids.[41] Very recently, de Koning used this strategy for the synthesis of indolizine alkaloids[42] and other research groups have produced indole analogues that inhibit tubulin polymerization.[43]

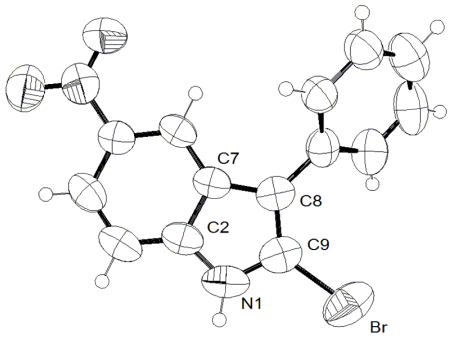
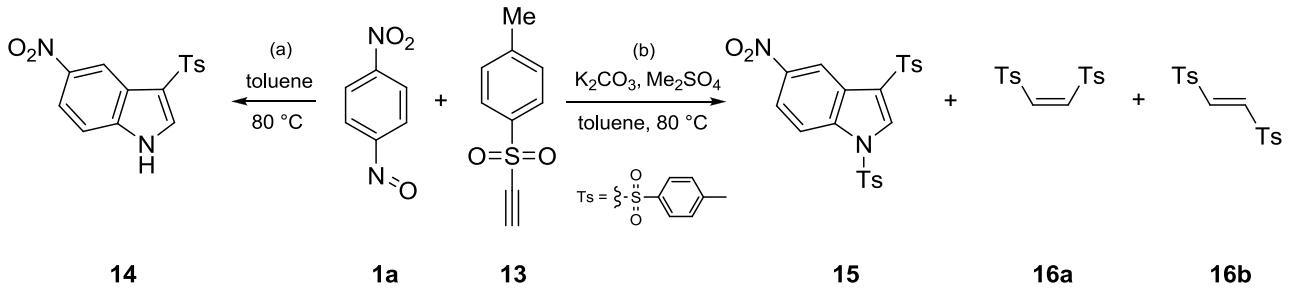


Figure 3. ORTEP drawing of the adduct **11a**, with partial labeling scheme. Thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms were given arbitrary radii. Significant bond distances (Å) and angles (°): N1-C2 1.358(5), C2-C7 1.407(5), C7-C8 1.438(6), C8-C9 1.367(5), C9-N1 1.364(6), C9-Br 1.856(5), N1-C9-Br 117.9(3), C8-C9-Br 130.8(4).

Evaluating another conjugated alkyne with the potential for subsequent further functionalization of the indole product we chose *p*-tosylacetylene to study its reaction with *p*-nitro-nitrosobenzene. Running the reaction without alkylative conditions led to the isolation of 5-nitro-3-tosylindole **14** in 31% yield (Scheme 10, path (a)). Studying the mass balance of the reaction we detected that most of 4-nitronitrosobenzene was converted to the corresponding azoxyarene; no traces of other byproducts were detected and unconverted *p*-tosylacetylene was recovered. The reaction under alkylating conditions showed the formation of a different adduct, the compound **15** in 25% yield with two tosyl groups (Scheme 10, path (b)). The characterization of compound **15** by ^{1}H- and ^{13}C-NMR initially did not lead us to an unambiguous structural assignment. However, X-ray diffraction analysis of **15** (Figure 4) identified its structure as *N*-Tosyl-3-tosyl-5-nitroindole resulting from loss of an ethyne molecule. Future studies will be carried out to clarify the mechanism of the reaction that produces **15**.



Scheme 10. Reactions between *p*-nitro-nitrosobenzene and *p*-tosylacetylene

It is noteworthy that a mixture of the diastereoisomers *Z*-ditosylethene **16a** and *E*-ditosylethene **16b** was obtained as a remarkable dimerization product of *p*-tosylacetylene with the loss of and ethyne fragment. These kinds of byproducts were afforded only by using the addition of a base. A previous paper on the preparation of **16a** and **16b** was reported by Carpino and coworkers.[44]

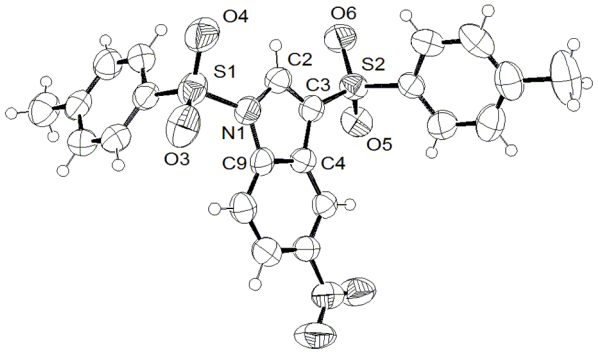
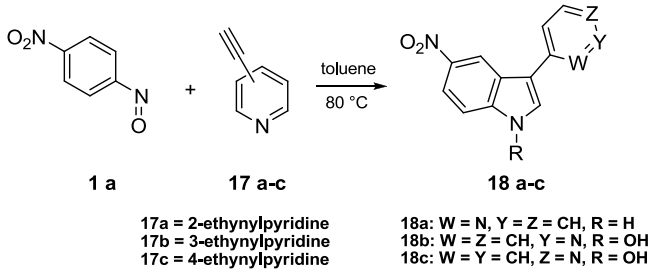


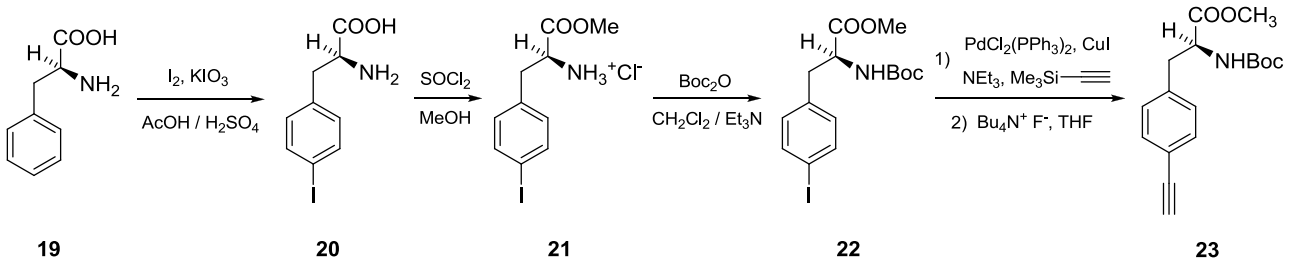
Figure 4. ORTEP drawing of the adduct **15**, with partial labeling scheme. Thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms were given arbitrary radii. Significant bond distances (Å) and angles (°): N1-C2 1.376(6), C2-C3 1.358(7), C3-C4 1.447(7), C4-C9 1.406(7), C9-N 1.399(6), N1-S1 1.703(4), C3-S2 1.736(5), C2-N1-S1 124.1(3), C2-C3-S2 125.0(4).

An interesting class of target molecules can be prepared using ethynylpyridines as reactants. The reactions were not carried out under alkylative or acylative conditions to avoid the obvious formation of pyridinium salts. One of the three 3-pyridinylindole products, compound **18c** obtained by the reaction with 4-ethynylpyridine is an analogue of a molecule that is under investigation for its activity as a Rho-kinase inhibitor[45] and an inosine monophosphate dehydrogenase inhibitor.[46] In all three cases the planned products were obtained in moderate to good yields with the primary formation of the corresponding indoles or *N*-hydroxyindoles (**18a**, 39%; **18b**, 46%; and **18c**, 57%) (Scheme 11).



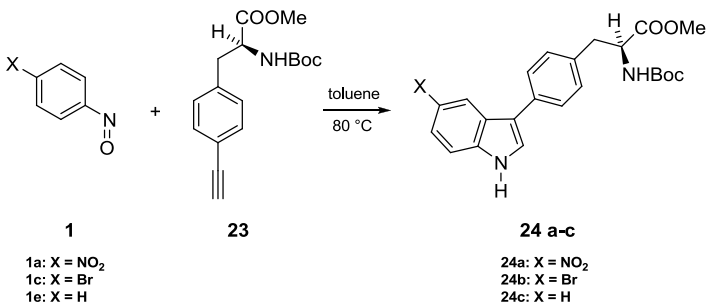
Scheme 11. Reactions between *p*-nitro-nitrosobenzene and substituted ethynylpyridines

Non proteinogenic indole aminoacids were also produced by the annulation of nitrosoarenes with alkynes. Unnatural amino acids are of interest for their widespread and enormous applications and several recent patents were published on their uses.[47] These aminoacids are deeply and frequently investigated in order to expand the chemical properties available in native enzymes through engineering t-RNA techniques. Unnatural aminoacids may be introduced to enhance and expand the chemical and biological properties in enzymes. Some changes in the primary structures can generate and modify different aspects as the acidity, the nucleophilicity, the H-bonding potential, etc. α-Amino acids with substituted aromatic ring are particularly interesting because they provide valuable tools in the developments of highly selective ligands since aromatic residues play a relevant role in molecular recognition processes.[48]



Scheme 12. Preparation of a terminal aromatic alkyne starting from Phenylalanine

Following a literature procedure[49] a more complicated and variously substituted terminal aromatic alkyne was obtained from phenylalanine through a multi-step synthetic strategy (Scheme 12). A selective iodination in *para* position by iodine/KIO_3 of Phe was carried out following protection of the COOH group as a methyl ester and of the amino group as a Boc amide.[49a] Then a Sonogashira reaction and cleavage of the trimethysilyl moiety by treatment with TBAF in THF led us to isolate the substrate **23**.[49b] The procedure provided the starting material on a large scale (5-10 g).



Scheme 13. Synthesis of indole derivatives containing the phenylalanine framework

Cycloaddition reactions of **23** with different nitrosoarenes were carried out and produced indole derivatives containing the phenylalanine unit as the major products (Scheme 13). The reactions were conducted without alkylating conditions and afforded the indole compounds **24a**, **24b** and **24c** in 55%, 47% and 50% yield respectively. Related compounds of this series of unnatural aminoacids were previously prepared by Ortar and co-authors by an efficient synthesis using Stille cross-coupling reaction with stannylated phenylalanines (4-trimethylstannylphenylalanines) as starting materials.[50] The products isolated by this procedure could be driven into amphiphilic environments.

CONCLUSIONS

A simple, efficient, highly regioselective, atom economical and one-pot method to prepare 3-substituted-*N*-hydroxyindole- and indole-derivatives via cycloaddition of nitrosoarenes with alkynes has been developed. Different protecting groups were used to facilitate the isolation of generally unstable and elusive *N*-*O*-protected hydroxyindoles by using a multi-component version. *N*-hydroxyindoles and *N*-methoxyindoles were afforded in good yields using conjugated alkynes (arylacetylenes and propiolates) in a substrate survey showing a general validity of the synthetic protocol. An unexpected synthesis of tricyclic aziridino-indolines from *o*-carbomethoxy-nitrosobenzene was discovered via the intermediacy of a nitrone that reacts with another molecule of alkyne. A natural expansion of the alkyne substrate scope was studied by reaction of nitrosoaromatics with 2-, 3- and 4-ethynylpyridine. An interesting synthetic application of the annulation of nitrosoaromatics with alkynes was tested in the synthesis of unnatural indole-derived aminoacids. Furthermore functionalizable indoles were achieved by using ethynyl-*p*-tolylsulfone and 1-bromo-2-phenylacetlene. Some aspects on the reaction mechanism are currently under investigation and particularly the electronic properties of the substituents on the nitrosoarene ring will be investigated. Future evaluations will be carried out through electrochemical experiments like cyclic voltammetry analyses and other techniques.

EXPERIMENTAL

General

All substituted anilines, nitrosobenzene (**1e**), methyl propiolate (**5**), phenylacetylene (**2g**), 4-ethynyltoluene (**2h**), ethynyl *p*-tolyl sulfone (**13**), phenylalanine (**19**), K_2CO_3, Me_2SO_4, Boc_2O, $PhCH_2Br$, Cbz-Cl, allyl bromide, benzoyl chloride, tosyl chloride, $ClCO_2Et$ were commercially available and were purchased from Sigma–Aldrich Chemical Co. and used directly. Distilled solvents were used for all the reactions. NMR spectra were obtained using the Bruker Avance 400 MHz spectrometer. Positive mode chemical ionization (CI) mass spectra (using isobutane as a reagent gas) were obtained by VG 7070 EQ mass spectrometer. GC–MS analyses were run on Shimadzu GC-MS-QP5000. IR spectra were obtained using the Nicolet Magna-IR Spectrometer 550. Before elemental analyses, all samples were kept under vacuum (< 1 mbar) at room temperature for 8-10 h. Elemental analyses were performed on a Perkin Elmer Series II CHNS/O Analyzer 2400. Uncorrected melting points were measured with a Büchi 535. Solid products were achieved by recrystalyzation using CH_2Cl_2/hexane.

Preparation of nitrosoarenes

4-Nitro-nitrosobenzene[31] (**1a**), 4-cyano-nitrosobenzene[31] (**1b**), 4-bromo-nitrosobenzene[51] (**1c**), 4-methoxy-nitrosobenzene[51] (**1f**), and 2-(carbomethoxy)-nitrosobenzene[51] (**1g**) were prepared as reported in the literature.

Nitroso-terephthalic acid dimethyl ester (**1d**)

The synthetic approach to **1d** reported here is a slight modification of a literature procedure using the oxidation of anilines with H_2O_2 and sodium tungstate.[51] To a solution of 2-aminoterephthalic acid dimethyl ester (2.09 g, 10.0 mmol) in ethanol (20 mL), sodium tungstate dihydrate (1.0 g, 3.4 mmol), phosphoric acid (1 mL of a 85% solution) and H_2O_2 (10 mL of a 30% solution) were added. The mixture was heated at 65° C until TLC (CH_2Cl_2–AcOEt=80:20) showed complete consumption of the aniline. The reaction mixture was then cooled to r.t and the solid precipitate was isolated by filtration, giving nitroso-terephthalic acid dimethyl ester as a pale yellow solid (1.77 g, 7.9 mmol, 79% yield), m.p.: 130 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (dd, 1H, ^{3}J = 7.9 Hz, ^{4}J = 1.6 Hz, H5), 7.98 (d, 1H, J = 7.9 Hz, H6), 7.44 (d, 1H, J = 1.6 Hz, H3), 4.08 (s, 3H, CO_2Me), 3.99 (s, 3H, CO_2Me). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 167.1, 164.9, 161.7, 134.8, 134.0, 133.3, 130.0, 113.5, 53.4, 52.9. MS (CI): m/z 224. IR (KBr, cm^{-1}): 2959, 1722, 1435, 1288, 758. Elemental Analysis: calcd C, 53.82; H, 4.06; N, 6.28; found C, 53.66; H, 4.09; N, 6.18.

Preparation of alkynes

1-Ethynyl-4-nitrobenzene[52] (**2a**), 4-ethynylbenzonitrile[53] (**2b**), 1-ethynyl-4-bromobenzene[54] (**2c**), 1-chloro-4-ethynylbenzene[55] (**2d**), 2-ethynylacetanilide[56] (**2e**), 4-ethynylacetanilide[57] (**2f**), 4-ethynyl-1-methoxybenzene[58] (**2i**) were prepared by Sonogashira-type reaction starting from the corresponding commercially available substituted haloarene (bromo- or iodoarene) following the procedure reported in literature. Compounds **10**[59], **17a**[60], **17b**[60], **17c**[61], **23**[49] were prepared as previously reported.

Representative synthesis of indole compounds 3a-q, 8a-b, 15

A mixture containing nitrosoarene (1.0 mmol), alkyne (12.0 mmol), K_2CO_3 (828 mg, 6.0 mmol), and Me_2SO_4 (570 µL, 6.0 mmol) in 80 mL of dry toluene was stirred at 80 °C for 4-12 h under nitrogen. After cooling to r.t., the mixture was filtered and the filtrate was concentrated by rotary evaporation. Flash chromatography of the residue over silica gel afforded the indole derivatives. Spectroscopic data are reported below.

Representative synthesis of indole compounds 4a-h, 6a-e

A mixture containing nitrosoarene (1.0 mmol), alkyne (12.0 mmol), K_2CO_3 (828 mg, 6.0 mmol), and protecting group precursor (6.0 mmol) in 80 mL of dry toluene was stirred at 80 °C for 5-8 h under nitrogen. After cooling to r.t., the mixture was filtered and the filtrate was concentrated by rotary evaporation. Flash chromatography of the residue over silica gel afforded the indole derivatives. Spectroscopic data are reported below.

Representative synthesis of indoline compounds 9a-h and of indole compounds 11a-b, 14, 18a-c, 24a-c

A mixture containing nitrosoarene (1.0 mmol), alkyne (12.0 mmol) in 80 mL of dry toluene was stirred at 80 °C for 4-8 h under nitrogen. After cooling to r.t., the mixture was filtered and the filtrate was concentrated by rotary evaporation. Flash chromatography of the residue over silica gel afforded the indole derivatives. Spectroscopic data are reported below.

*1-Methoxy-5-nitro-3-(4-nitrophenyl)-1H-indole (**3a**).*
Reaction time: 4 h. Flash chromatography (hexane/ethyl acetate=75:25). Yellow prism, m.p.: 216-218 °C yield = 91%, (286 mg, 0.91 mmol). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.87 (d, 1H, J = 1.5 Hz, H4), 8.37 (d, 2H, J = 8.6 Hz, H3' and H5'), 8.28 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 1.5 Hz, H6), 7.80 (d, 2H, J = 8.6 Hz, H2' and H6'), 7.76 (s, 1H, H2), 7.61 (d, 1H, J=9.0 Hz, H7), 4.26 (s, 3H, N-OMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 143.2, 140.0, 135.0, 130.9, 128.8, 127.7, 124.6, 124.4, 120.8, 119.0, 117.3, 109.0, 67.0. IR (KBr, cm^{-1}): ν = 2962, 1727, 1598, 1512, 1337, 1261, 1095, 1020, 800 cm^{-1}. MS (CI): *m/z*: 314 [*M*+1]. Elemental analyses for $C_{15}H_{11}N_3O_5$: calcd (%) C 57.51, H 3.54, N 13.41 found (%): C 57.32, H 3.43, N 13.17.

*4-(1-methoxy-5-nitro-1H-indol-3-yl)benzonitrile (**3b**)*
Reaction time: 4 h. Flash chromatography (Hexane-EtOAc=70:30, Rf=0.35). Light brown prism, m.p.: 166-168 °C, yield = 82%, (241 mg, 0.82 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.88 (d, 1H, J = 2.0 Hz, H4), 8.38 (d, 2H, J = 8.7 Hz, H3' and H5'), 8.28 (dd, 1H, ^{3}J = 8.9 Hz, ^{4}J = 2.0 Hz, H6), 7.80 (d, 2H, J = 8.7 Hz, H2' and H6'), 7.76 (s, 1H, H2), 7.61 (d, 1H, J = 8.9 Hz, H7), 3.98 (s, 3H, N-OMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 138.7, 133.0, 130.9, 129.9, 128.8, 127.8, 126.1, 124.4, 124.1, 123.9, 119.0, 117.3, 109.0, 67.0. IR (KBr, cm^{-1}): ν = 2925, 2854, 2227, 1728, 1599, 1520, 1466, 1336, 1111, 1072, 850 cm^{-1}. MS (CI): *m/z*: 294 [*M*+1]. Elemental analyses for $C_{16}H_{11}N_3O_3$: calcd (%) C 65.53, H 3.78, N 14.33 found (%): C 65.32, H 3.84, N 14.12.

*3-(4-Bromophenyl)-1-methoxy-5-nitro-1H-indole (**3c**)*
Reaction time: 5 h. Flash chromatography (CH_2Cl_2-Hexane=40:60). Light brown prism, m.p. 193-195 °C yield = 77%, (267 mg, 0.77 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.81 (s, 1H, H4), 8.24 (d, 1H, J = 9.1 Hz, H6), 7.64 (d, 2H, J = 8.0 Hz, H3' and H5'), 7.59 (s, 1H, H2), 7.55 (d, 1H, J = 9.1 Hz, H7), 7.50 (d, 2H, J = 8.0 Hz, H2' and

H6'), 4.22 (s, 3H, N-OMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 143.1, 135.3, 132.7, 132.5, 129.6, 123.4, 121.6, 121.5, 119.0, 117.9, 116.0, 109.0, 67.1. IR (KBr, cm^{-1}): ν = 2941, 1517, 1466, 1327, 1301, 1061, 833, 797 cm^{-1}. MS (CI): *m/z*: 348/346 [*M*+1]. Elemental analyses for $C_{15}H_{11}BrN_2O_3$: calcd (%) C 51.90, H 3.19, N 8.07 found (%): C 52.01, H 3.07, N 8.23.

*3-(4-Chlorophenyl)-1-methoxy-5-nitro-1H-indole (**3d**)*

Reaction time: 4,5 h. Flash chromatography (CH_2Cl_2/Hexane=50:50). Yellow plate, m.p. 169-170 °C yield = 67%, (203 mg, 0.67 mmol). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.80 (d, 1H, J = 1.6 Hz, H4), 8.23 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 1.6 Hz, H6), 7.58 (s, 1H, H2), 7.57 – 7.54 (m, 3H, H3' and H5' + H7), 7.48 (d, 2H, J = 8.4 Hz, H2' and H6'), 4.22 (s, 3H, N-OMe). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.73 (d, 1H, J = 2.1 Hz, H4), 8.43 (s, 1H, H2), 8.18 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.77 – 7.75 (m, 3H, H3' and H5' + H7), 7.58 (d, 2H, J = 8.5 Hz, H2' and H6') 4.21 (s, 3H, N-OMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 143.1, 135.2, 133.5, 132.0 , 129.9, 129.4, 123.5, 121.6, 119.0, 117.9, 116.1, 109.0, 67.1. IR (KBr, cm^{-1}): ν = 2921, 2851, 1518, 1465, 1327, 1302, 1062, 837, 796 cm^{-1}. MS (CI): *m/z*: 305/303 [*M*+1 (^{37}Cl/^{35}Cl)]. Elemental analyses for $C_{15}H_{11}ClN_2O_3$: calcd (%) C 59.52, H 3.66, N 9.25 found (%): C 59.42, H 3.75, N 8.99.

*N-(2-(1-methoxy-5-nitro-1H-indol-3-yl)phenyl)ethanamide (**3e**)*

Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =40:60).Yellow prism, m.p. 78-80 °C, yield = 37%, (121 mg, 0.37 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.39 (d, 1H, J = 2.0 Hz, H4), 8.24 (d, 1H, J = 8.0 Hz, H3'), 8.15 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.0 Hz, H6), 7.56 (s, 1H, H2), 7.55 (d, 1H, J = 9.0 Hz, H7), 7.43 – 7.35 (m, 3H, H4'+ H6'+NHC(O)Me), 7.24 (t, 1H, J = 8.0 Hz, H5'), 4.24 (s, 3H, N-OMe), 1.99 (s, 3H, NHC(O)Me). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.9, 142.9, 136.1, 134.9, 131.4, 129.2, 125.2, 125.1, 123.5, 123.1, 122.4, 119.1, 117.8, 112.2, 109.1, 67.3, 24.8. IR (KBr, cm^{-1}): ν = 3283, 2924, 2853, 1669, 1582, 1516, 1447, 1372, 1331, 1301, 1064, 751 cm^{-1}. MS (CI): *m/z*: 326 [*M*+1]. Elemental analyses for $C_{17}H_{15}N_3O_4$: calcd (%) C 62.76, H 4.65, N 12.92 found (%): C 62.57, H 4.53, N 13.08.

*N-(4-(1-Methoxy-5-nitro-1H-indol-3-yl)phenyl)ethanamide (**3f**)*

Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =40:60. Yellow oil, yield = 55%, (179 mg, 0.55 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 10.5 (s, 1H, NHC(O)Me), 8.69 (d, 1H, J = 2.0 Hz, H4), 8.25 (s, 1H, H2), 8.11 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.0 Hz, H6), 7.73 (d, 2H, J = 8.6 Hz, H2' and H6'), 7.69 (d, 1H, J = 9.0 Hz, H7), 7.62 (d, 2H, J = 8.6 Hz, H3' and H5'), 4.18 (s, 3H, N-OMe), 2.09 (s, 3H, NHC(O)Me). ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 169.2, 142.6, 139.1 135.1, 128.3, 127.9, 125.4, 121.1, 120.4, 118.6, 117.7, 115.8, 109.9, 67.6, 24.9. IR (film, cm^{-1}): ν = 3280, 2928, 2855, 1661, 1578, 1520, 1443, 1376, 1328, 1302, 1064, 759 cm^{-1}. MS (CI): *m/z*: 326 [*M*+1]. Elemental analyses for $C_{17}H_{15}N_3O_4$: calcd (%) C 62.76, H 4.65, N 12.92 found (%): C 63.04, H 4.78, N 13.01.

*1-Methoxy-5-nitro-3-p-tolyl-1H-indole (**3g**)*

Reaction time: 4 h. Flash chromatography (Hexane- EtOAc =90:10). Orange prism, m.p. 98-100 °C, yield = 48%, (136 mg, 0.48 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.84 (d, 1H, J = 2.1 Hz, H4), 8.21 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.56 (s, 1H, H2), 7.53 (d, 1H, J = 9.0 Hz, H7), 7.51 (d, 2H, J = 7.9 Hz, H2' and H6'), 7.31 (d, 2H, J = 7.9 Hz, H3' and H5'), 4.20 (s, 3H, N-OMe), 2.44 (s, 3H, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): 142.4, 137.0, 134.7, 130.1, 129.8, 127.6, 122.6, 121.4, 118.3, 117.9, 116.8, 108.4, 66.6, 21.2. IR(KBr, cm^{-1}): ν = 2921, 1606, 1518, 1467, 1331, 1310, 1064, 811, 737 cm^{-1}. MS (CI): *m/z*: 283 [*M*+1]. Elemental analyses for $C_{16}H_{14}N_2O_3$:

calcd (%) C 68.07, H 5.00, N 9.92 found (%):C 67.84, H 4.81, N 9.98.

*1-Methoxy-3-(4-methoxyphenyl)-5-nitro-1H-indole (**3h**)*

Reaction time: 4 h. Flash chromatography (Toluene-hexane=80:20). Yellow needle, m.p. 142-144 °C yield = 76%, (226 mg, 0.76 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.68 (d, 1H, J = 2.1 Hz, H4), 8.25 (s, 1H, H2), 8.15 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.73 (d, 1H, J = 9.0 Hz, H7), 7.68 (d, 2H, J = 8.7 Hz, H2' + H6'), 7.10 (d, 2H, J = 8.7 Hz, H3' + H5'), 4.20 (s, 3H, N-OMe), 3.82 (s, 3H, OMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 159.0, 142.4, 134.7, 128.9, 125.5, 122.3, 121.4, 118.3, 117.8, 116.6, 114.6, 108.3, 66.6, 55.4. MS (CI): *m/z*: 298 [*M*+1]. IR(KBr, cm^{-1}): ν = 2923, 2851, 1612, 1549, 1517, 1465, 1330, 1248, 1065, 1032, 804, 735 cm^{-1}. Elemental analyses for $C_{16}H_{14}N_2O_4$: calcd (%) C 64.42, H 4.73, N 9.39 found (%): C 64.27, H 4.71, N 9.45.

*1-Methoxy-3-phenyl-1H-indole-5-carbonitrile (**3i**)*

Reaction time: 7 h. Flash chromatography (Hexane- EtOAc =90:10). Orange plate, m.p. 101-103 °C, yield = 57%, (142 mg, 0.57 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.40 (d, 1H, J = 1.2 Hz, H4), 8.31 (s, 1H, H2), 7.74 – 7.72 (m, 3H, H7 and H2' + H6'), 7.64 (dd, 1H, ^{3}J = 8.5 Hz, ^{4}J = 2.1 Hz, H6), 7.48 (t, 2H, J = 7.6 Hz, H3' + H5'), 7.33 (t, 1H, J = 7.4 Hz, H4'), 4.18 (s, 3H, N-OMe). ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 134.1, 129.9, 128.0, 127.4, 126.4, 126.2, 125.0, 121.6, 121.1, 114.3, 110.7, 103.8, 67.6. MS (CI): *m/z*: 249 [*M*+1]. IR(KBr, cm^{-1}): ν = 2940, 2221, 1604, 1463, 1067, 805, 761 cm^{-1}. Elemental analyses for $C_{16}H_{12}N_2O$: calcd (%) C 77.40, H 4.87, N 11.28 found (%): C 77.13, H 4.95, N 11.39.

*5-Bromo-1-methoxy-3-phenyl-1H-indole (**3j**)*

Reaction time: 8 h. Flash chromatography (Hexane- EtOAc =80:20). Yellow plate, m.p. 58-60 °C, yield = 47%, (142 mg, 0.47 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.13 (s, 1H, H2), 8.00 (d, 1H, J = 1.8 Hz, H4), 7.66 (d, 2H, J = 7.4 Hz, H2' + H6'), 7.53 (d, 1H, J = 8.7 Hz, H7), 7.46 (t, 2H, J = 7.4 Hz, H3' + H5'), 7.41 (dd, 1H, ^{3}J = 8.7 Hz, ^{4}J = 1.8 Hz, H6), 7.29 (t, 1H, J = 7.4 Hz, H4'), 4.14 (s, 3H, N-OMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 134.6, 131.6, 129.0, 127.9, 126.9, 126.1, 124.1, 123.1, 121.8, 114.3, 114.0, 110.4, 66.6. MS (CI): *m/z*: 304/302 [*M*+1]. IR(KBr, cm^{-1}): ν = 2935, 1674, 1598, 1488, 1452, 1287, 1249, 1069, 795, 699 cm^{-1}. Elemental analyses for $C_{15}H_{12}BrNO$: calcd (%) C 59.62, H 4.00, N, 4.64 found (%): C 59.39, H 4.11, N 4.17.

*Dimethyl 1-methoxy-3-phenyl-1H-indole-4,7-dicarboxylate (**3k**)*

Reaction time: 7 h. Flash chromatography (Hexane- EtOAc =85:15). Orange prism, m.p. 77-79 °C, yield = 62%, (211 mg, 0.62 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, 1H, J = 7.6 Hz, H5), 7.52 (d, 1H, J = 7.6 Hz, H6), 7.45 (s, 1H, H2), 7.42 (d, 2H, J = 7.4 Hz, H2' + H6'), 7.34 (m, 3H, H3' +H4' + H5'), 4.16 (s, 3H, N-OMe), 4.03 (s, 3H, COOMe), 3.98 (s, 3H, COOMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.8, 167.6, 145.3, 141.3, 137.3, 135.9, 128.8, 128.7, 127.0, 125.9, 124.1, 122.0, 119.1, 116.3, 66.8, 53.4, 51.8. MS (CI): *m/z*: 340 [*M*+1]. IR(KBr, cm^{-1}): ν = 2948, 1752, 1725, 1434, 1274, 1164, 1139, 746 cm^{-1}. Elemental analyses for $C_{19}H_{17}NO_5$: calcd (%) C 67.25, H 5.05, N 4.13 found (%): C 67.42, H 4.95, N 4.17.

*1-Methoxy-3-(4-nitrophenyl)-1H-indole (**3l**)*

Reaction time: 9 h. Flash chromatography (hexane- EtOAc =75:25). Orange oil, yield = 41%, (110 mg, 0.41 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, 2H, J = 8.8 Hz, H3' + H5'), 7.95 (d, 1H, J = 8.2 Hz, H4), 7.80 (d, 2H, J = 8.8 Hz, H2' + H6'), 7.62 (s, 1H, H2), 7.55 (d, 1H, J = 8.2 Hz, H7), 7.38 (m, 1H, H5), 7.29 (m, 1H, H6), 4.20 (s, 3H, N-OMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 147.9, 133.5, 131.6, 128.4, 126.4, 124.4, 121.8, 121.4, 120.0, 119.8, 110.1, 108.2, 66.3. MS (CI): *m/z*: 269 [*M*+1]. GC-MS (EI): *m/z*: 268 [M^{+}], 253, 237, 221, 207, 194, 180,

165, 151, 139, 132, 111, 102, 82, 76, 63. IR (film, cm^{-1}): ν = 2935, 2840, 1610, 1544, 1500, 1451, 1243, 1180, 1033, 836, 750 cm^{-1}. Elemental analyses for $C_{15}H_{12}N_2O_3$: calcd (%) C 67.16, H 4.51, N 10.44 found (%): C 67.29, H 4.64, N 10.32.

*4-(1-Methoxy-1H-indol-3-yl)benzonitrile (**3m**)*

Reaction time: 8,5 h. Flash chromatography (Hexane- EtOAc =80:20, Rf=0.32). Yellow brown oil, yield = 39%, (97 mg, 0.39 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, 1H, J = 8.0 Hz, H4), 7.76 (d, 2H, J = 8.5 Hz, H3' + H5'), 7.72 (d, 2H, J = 8.5 Hz, H2' + H6'), 7.57 (s, 1H, H2), 7.54 (d, 1H, J = 8.0 Hz, H7), 7.36 (t, 1H, J = 8.0 Hz, H5), 7.26 (d, 1H, J = 8.0 Hz, H6), 4.19 (s, 3H, N-OMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 133.0, 132.6, 128.5, 127.4, 126.3, 123.3, 121.5, 121.4, 119.7, 119.3, 112.0, 110.4, 108.9, 66.3. MS (CI): *m/z*: 249 [*M*+1]. IR (film, cm^{-1}): ν = 2918, 2849, 2228, 1740, 1604, 1462, 1260, 1067, 909, 800, 732 cm^{-1}. Elemental analyses for $C_{16}H_{12}N_2O$: calcd (%) C 77.40, H 4.87, N 11.28 found (%) C 77.61, H 4.85, N 11.09.

*3-(4-Chlorophenyl)-1-methoxy-1H-indole (**3n**)*

Reaction time: 10 h. Flash chromatography (CH_2Cl_2- EtOAc =80:20, Rf=0.30). Pale brown oil, yield = 29%, (75 mg, 0.29 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, 1H, J = 7.8 Hz, H4), 7.54 (d, 1H, J = 7.8 Hz, H7), 7.46 (s, 1H, H2), 7.50 (d, 2H, J = 8.5 Hz, H3' + H5'), 7.38 (d, 2H, J = 8.5 Hz, H2' + H6'), 7.09 (t, 1H, J = 7.8 Hz, H5), 7.21 (t, 1H, J = 7.8 Hz, H6), 3.81 (s, 3H, N-OMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 135.5, 133.4, 128.9, 128.81 125.8, 122.9, 121.6, 120.8, 120.5, 119.8, 112.7, 108.6, 68.1. MS (CI): *m/z*: 260/258 [*M*+1 (^{37}Cl/^{35}Cl)]. IR (film, cm^{-1}): ν = 2933, 2836, 1609, 1549, 1503, 1454, 1244, 1178, 1033, 834, 741 cm^{-1}. Elemental analyses for $C_{15}H_{12}ClNO$: calcd (%) C 69.91, H 4.69, N 5.43 found (%) C 69.87 H 4.76 N 5.39.

*1-Methoxy-3-p-tolyl-1H-indole (**3o**)*

Reaction time: 8 h. Flash chromatography (Hexane- EtOAc =90:10). Orange oil, yield = 46%, (109 mg, 0.46 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.95 (dt, 1H, ^{3}J = 8.0 Hz, ^{4}J = 0.8 Hz, H4), 7.59 (d, 2H, J = 8.1 Hz, H3' + H5'), 7.53 (dt, 1H, ^{3}J = 8.0 Hz, ^{4}J = 0.8 Hz, H7), 7.46 (s, 1H, H2), 7.34 (td, 1H, ^{3}J = 8.0 Hz, ^{4}J = 0.8 Hz, H6), 7.31 (d, 2H, J = 8.1 Hz, H2' + H6'), 7.23 (td, 1H, ^{3}J = 8.0 Hz, ^{4}J = 0.8 Hz, H5), 4.17 (s, 3H, N-OMe), 2.45 (s, 3H, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 136.2, 133.1, 132.4, 129.9, 127.9, 123.1, 122.7, 120.9, 120.7, 120.6, 114.4, 108.9, 66.3, 21.6. MS (CI): *m/z*: 238 [*M*+1]. IR (film, cm^{-1}): ν = 2934, 1662, 1549, 1452, 1323, 1256, 1064, 967, 824, 740, 686 cm^{-1}. Elemental analyses for $C_{16}H_{15}NO$: calcd (%) C 80.98, H 6.37, N 5.90 found (%) C 81.11, H 6.42, N 5.78.

*1-Methoxy-3-(4-methoxyphenyl)-1H-indole (**3p**)*

Reaction time: 8 h. Flash chromatography (Toluene-hexane=60:40). Orange-brown oil, yield = 35%, (89 mg, 0.35 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, 1H, J = 7.8 Hz, H4), 7.59 (d, 2H, J = 8.6 Hz, H3' + H5'), 7.51 (d, 1H, J = 7.8 Hz, H7), 7.40 (s, 1H, H2), 7.32 (t, 1H, J = 7.8 Hz, H6), 7.21 (t, 1H, J = 7.8 Hz, H5), 7.03 (d, 2H, J = 8.6 Hz, H2' + H6'), 4.13 (s, 3H, N-OMe), 3.89 (s, 3H, OMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 158.2, 132.7, 128.7, 127.4, 122.7, 122.3, 120.4, 120.0, 120.0, 114.3, 113.6, 108.5, 65.9, 55.4. MS (CI): *m/z*: 254 [*M*+1]. IR (film, cm^{-1}): ν = 2933, 2836, 1609, 1548, 1502, 1454, 1244, 1178, 1033, 966, 834, 740 cm^{-1}.

Elemental analyses for $C_{16}H_{15}NO_2$: calcd (%) C 75.87, H 5.97, N 5.53 found (%) C 76.03, H 6.05, N 5.59.

*1,5-Dimethoxy-3-phenyl-1H-indole (**3q**)*

Reaction time: 12 h. Flash chromatography (Hexane- EtOAc =90:10). Colourless oil, yield = 25%, (63 mg, 0.25

mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, 2H, J = 7.6 Hz, H2' + H6'), 7.49 (t, 2H, J = 7.6 Hz, H3' + H5'), 7.44 (s, 1H, H2), 7.41 (m, 2H, H7 + H4), 7.33 (t, 1H, J = 7.6 Hz, H4'), 7.01 (d, 1H, J = 8.9 Hz, H6), 4.15 (s, 3H, N-OMe), 3.90 (s, 3H, OMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 155.5, 135.5, 129.3, 129.2, 127.8, 126.5, 123.1, 121.6, 113.9, 113.5, 109.9, 102.3, 66.4, 56.4. MS (CI): *m/z*: 254 [*M*+1]. IR (film, cm^{-1}): ν = 2936, 2832, 1602, 1475, 1441, 1260, 1223, 1174, 1109, 1032, 970, 759, 699 cm^{-1}. Elemental analyses for $C_{16}H_{15}NO_2$: calcd (%) C 75.87, H 5.97, N 5.53 found (%) C 76.01, H 5.72, N 5.64.

*Tert-butyl 5-nitro-3-phenyl-1H-indol-1-yl carbonate (**4a**)*

Reaction time: 5 h. Flash chromatography (hexane-CH_2Cl_2=30:70). Orange prism, m.p. 121-123 °C, yield = 65%, (231 mg, 0.65 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.85 (d, 1H, J = 2.1 Hz, H4), 8.23 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.63 (d, 2H, J = 7.5 Hz, H2' + H6'), 7.53 (s, 1H, H2), 7.50 (t, 2H, J = 7.5 Hz, H3' + H5'), 7.38 (m, 2H, H7 + H4'), 1.55 (s, 9H, CMe_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.7, 143.4, 136.6, 133.0, 129.5, 128.3, 127.8, 124.8, 122.2, 119.4, 118.1, 117.9, 109.0, 85.6, 27.8. MS (CI): *m/z*: 355 [*M*+1]. IR (KBr, cm^{-1}): ν = 3099, 2973, 1735, 1619, 1522, 1469, 1337, 1070, 751, 699 cm^{-1}. Elemental analyses for $C_{19}H_{18}N_2O_5$: calcd (%) C 64.40, H 5.12, N 7.91 found (%) C 64.27, H 5.01, N 7.68.

*1-Benzyloxyl 5-nitro-3-phenyl-1H-indole (**4b**)*

Reaction time: 5 h. Flash chromatography (hexane-CH_2Cl_2=30:70). Yellow plate, m.p. 104-106 °C, yield = 77%, (266 mg, 0.77 mmol). ^{1}H-NMR (400 MHz, DMSO): δ = 8.69 (d, 1H, J = 2.1 Hz, H4), 8.26 (s, 1H, H2), 8.07 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.68 (d, 2H, J = 7.2 Hz, H2' + H6'), 7.57 (d, 1H, J = 9.0 Hz, H7), 7.51 (m, 4H, CH_2Ph), 7.40 (m, 3H, H3' + H4' + H5'), 7.36 (t, 1H, J = 7.2 Hz, CH_2Ph), 5.41 (s, 2H, CH_2Ph). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 142.4, 135.4, 133.8, 133.1, 129.9, 129.8, 129.1, 128.9, 127.7, 127.13, 124.1, 121.2, 118.2, 117.6, 116.4, 108.7, 81.2. MS (CI): *m/z*: 345 [*M*+1]. IR (KBr, cm^{-1}): ν = 2919, 1603, 1517, 1332, 1288, 1064, 747, 698 cm^{-1}. Elemental analyses for $C_{21}H_{16}N_2O_3$: calcd (%)C, 73.24; H, 4.68; N, 8.13 found (%) C 73.51, H 4.79, N 8.02.

*Ethyl 5-nitro-3-phenyl-1H-indol-1-yl carbonate (**4c**)*

Reaction time: 5 h. Flash chromatography (Hexane-CH_2Cl_2=50:50). Orange prism, m.p. 71-73 °C yield = 61%, (199 mg, 0.61 mmol). ^{1}H-NMR (400 MHz $CDCl_3$): δ = 8.87 (d, 1H, J = 2.1 Hz, H4), 8.25 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.64 (d, 2H, J = 7.5 Hz, H2' + H6'), 7.53 (m, 3H, H3' + H5' + H2), 7.42 (m, 2H, H4' + H7), 4.51 (q, 2H, J = 7.1.0 Hz, $CO_2CH_2CH_3$), 1.51 ppm (t, 3H, J = 7.1 Hz, $CO_2CH_2CH_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 153.9, 143.5, 136.7, 132.9, 129.6, 128.3, 128.0, 124.6, 122.4, 119.6, 118.3, 118.1, 109.0, 68.1, 14.6. MS (CI): *m/z*: 327 [*M*+1]. IR (KBr, cm^{-1}): ν = 3087, 2922, 2852, 1803, 1736, 1606, 1522, 1470, 1339, 1232, 1071, 837, 737, 700 cm^{-1}. Elemental analyses for $C_{17}H_{14}N_2O_5$: calcd (%) C 62.57, H 4.32, N 8.59 found (%) C 62.68, H 4.44, N 8.64.

*Benzyl 5-nitro-3-phenyl-1H-indol-1-yl carbonate (**4d**)*

Reaction time: 5 h. Flash chromatography (Hexane-CH_2Cl_2=50:50). Orange prism, m.p. 99-101 °C, yield = 53%, (206 mg, 0.53 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.86 (d, 1H, J = 2.0 Hz, H4), 8.23 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.0 Hz, H6), 7.63 (d, 2H, J = 7.2 Hz, H2' + H6'), 7.54 - 7.46 (m, 8H, H2 + H3' + H5' + Ph (Cbz group)), 7.41 (t, 1H, J = 7.3 Hz, H4'), 7.37 (d, 1H, J = 9.0 Hz, H7), 5.43 (s, 2H, CH_2Ph (Cbz group)). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 153.9, 143.6, 136.7, 133.7, 132.8, 130.0, 129.6, 129.4, 129.3, 128.3, 128.0, 124.6, 122.5, 119.6, 118.4, 118.1, 109.1, 73.4. MS (CI): *m/z*: 389 [*M*+1]. IR (KBr, cm^{-1}): ν = 2923, 2853, 1734, 1604, 1521, 1473, 1338, 1262, 1074, 838, 738, 699 cm^{-1}. Elemental analyses for $C_{22}H_{16}N_2O_5$: calcd (%) C 68.04, H 4.15, N 7.21 found (%) C

68.23, H 4.28, N 7.05.

*1-(Allyloxy)-5-nitro-3-phenyl-1H-indole (**4e**)*

Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =70:30). Orange needles, m.p. 85-87 °C, yield = 86%, (254 mg, 0.86 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.84 (d, 1H, J = 1.9 Hz, H4), 8.18 (dd, 1H, ^{3}J = 8.2 Hz, ^{4}J = 1.9 Hz, H6), 7.61 (d, 2H, J = 8.2 Hz, H2' + H6'), 7.56 (s, 1H, H2), 7.52 – 7.48 (m, 3H, H7 and H3' + H5'), 7.37 (t, 1H, J = 7.4 Hz, H4'), 6.15 (m, 1H, $CH_2CH=CH_2$), 5.41 (dd, 2H, J = 13.5 Hz, J = 5.2 Hz, $CH_2CH=CH_2$), 4.80 (d, 2H, J = 6.6 Hz, $CH_2CH=CH_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 142.8, 135.9, 135.5, 131.2, 129.6, 128.1, 127.6, 124.5, 123.3, 121.6, 118.7, 118.1, 116.8, 109.3, 80.4. MS (CI): *m/z*: 295 [*M*+1]. IR (KBr, cm^{-1}): ν = 2930, 1886, 1577, 1518, 1468, 1333, 1288, 1065, 941, 900, 864, 747, 699 cm^{-1}. Elemental analyses for $C_{17}H_{14}N_2O_3$: calcd (%) C 69.38, H 4.79, N 9.52 found (%) C 69.51, H 4.65, N 9.48.

*5-nitro-3-phenyl-1H-indol-1-yl-4-methylbenzenesulfonate (**4f**)*

Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =80:20). Brown oil, yield = 32%, (131 mg, 0.32 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.57 (d, 1H, J = 2.4 Hz, H4), 8.20 (dd, 1H, ^{3}J = 9.1 Hz, ^{4}J = 2.4 Hz, H6), 7.51 (m, 2H, H7 + H2), 7.38 (d, 2H, J = 8.3 Hz, H2'' + H6'' (Ts group)), 7.29 – 7.25 (m, 3H, H2' + H6' and H4'), 7.15 (m, 2H, H3' + H5'), 6.94 (d, 2H, J = 8.3 Hz, H3'' + H5'' (Ts group)), 2.50 (s, 3H, $SO_2C_6H_4$-Me). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 146.8, 146.2, 145.0, 144.7, 133.8, 130.9, 130.8, 130.1, 129.9, 128.9, 128.7, 128.5, 127.0, 124.1, 123.3, 114.0, 21.8. IR (film, cm^{-1}): ν = 3064, 2924, 2854, 1760, 1597, 1526, 1341, 1258, 1150, 1082, 750, 699 cm^{-1}.MS (CI): *m/z*: 409 [*M*+1]. Elemental Analysis for $C_{21}H_{16}N_2O_5S$: calcd (%) C 61.76; H, 3.95; N, 6.86 found (%) C 61.88, H 4.04, N 6.99.

*1-(Allyloxy)-3-phenyl-1H-indole-5-carbonitrile (**4g**)*

Reaction time: 7 h. Flash chromatography (Hexane- EtOAc =90:10). Orange prism, m.p. 83-85 °C, yield = 44%, (121 mg, 0.44 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.38 (m, 1H, H4), 8.25 (s, 1H, H2), 7.72 (m, 3H, H7 and H2' + H6'), 7.63 (dd, 1H, ^{3}J = 8.5 Hz, ^{4}J = 1.4 Hz, H6), 7.47 (t, 2H, ^{3}J = 8.0 Hz, H3' + H5'), 7.37 (tt, 1H, ^{3}J = 7.4 Hz, ^{4}J = 1.2 Hz, H4'), 6.20 (m, 1H, $CH_2CH=CH_2$), 5.40 (dd, 2H, J = 17.1 Hz, J = 1.2 Hz, $CH_2CH=CH_2$), 5.33 (dd, 2H, J = 10.2 Hz, J = 1.2 Hz, $CH_2CH=CH_2$), 4.87 (d, 2H, J = 6.6 Hz, $CH_2CH=CH_2$). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.38 (d, 1H, J = 1.4 Hz), 8.26 (s, 1H), 7.74 – 7.71 (m, 3H), 7.63 (dd, 1H, ^{3}J = 8.5 Hz, ^{4}J = 1.4 Hz), 7.48 (tt, 2H, ^{3}J = 7.7 Hz, ^{4}J = 1.6 Hz), 7.33 (tt, 1H, ^{3}J = 7.7 Hz, ^{4}J = 1.6 Hz), 6.19 (m, 1H), 5.39 (dq, 1H, J = 17.1 Hz, J = 1.3 Hz), 5.33 (dq, 1H, J = 10.3 Hz, J = 1.0 Hz), 4.88 (dt, 2H, ^{3}J = 6.6 Hz, ^{4}J = 1.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 134.8, 133.8, 131.3, 129.5, 128.1, 127.4, 126.3, 125.8, 123.8, 123.1, 122.1, 120.9, 115.1, 110.1, 104.1, 80.2. MS (CI): *m/z*: 275 [*M*+1]. IR (KBr, cm^{-1}): ν = 2924, 2216, 1867, 1606, 1544, 1469, 1371, 1207, 1069, 945, 800, 694 cm^{-1}. Elemental analyses for $C_{18}H_{14}N_2O$: calcd (%) C 78.81, H 5.14, N 10.21 found (%) C 78.73, H 5.09, N 9.98.

*1-(Benzoyloxy)-5-cyano-3-phenyl-1H-indole (**4h**)*

Reaction time: 8 h. Flash chromatography (Hexane-EtOAc =90:10). Orange oil, yield = 38%, (129 mg, 0.38 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.45 (d, 1H^{4}J = 1.4 Hz, H4), 8.32 (m, 1H, H7), 8.24 (dd, 2H, ^{3}J = 7.1 Hz, ^{4}J = 1.4 Hz, H2'' + H6''), 7.87 (tt, 1H, ^{3}J = 7.4 Hz, ^{4}J = 1.4 Hz, H4''), 7.76 – 7.68 (m, 4H, H2' + H6' and H3'' + H5''), 7.70 (s, 1H, H2), 7.64 (dd, 1H, ^{3}J = 8.5 Hz, ^{4}J = 1.4 Hz, H6), 7.50 (tt, 2H, ^{3}J = 7.4 Hz, H3' + H5'), 7.36 (tt, 1H, ^{3}J = 7.4 Hz, ^{4}J = 1.2 Hz, H4'). ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 165.0, 136.2, 135.9, 133.6, 131.1, 130.2, 129.9, 128.1, 127.7, 126.9, 126.7, 126.4, 126.2, 122.3, 120.8, 115.4, 111.2, 104.6. IR (film, cm^{-1}): ν = 3064, 2918, 2855, 2228, 1731, 1690, 1606, 1520, 1473, 1339, 1260, 1074, 840, 739, 700 cm^{-1}. MS (CI): *m/z*: 339 [*M*+1]. Elemental analyses for $C_{22}H_{14}N_2O_2$: calcd (%) C 78.09, H 4.17, N 8.28 found (%) C 77.89, 4.22, N 8.37.

*Methyl 1-(ethoxycarbonyloxy)-5-nitro-1H-indole-3-carboxylate (**6a**)*

Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =80:20). Yellow plate, m.p. 119-121 °C, yield = 73%, (226 mg, 0.73 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.09 (d, 1H, J = 2.1 Hz, H4), 8.23 (dd, 1H, ^{3}J = 9.1 Hz, ^{4}J = 2.1 Hz, H6), 8.05 (s, 1H, H2), 7.41 (d, 1H, J = 9.1 Hz, H7), 4.50 (q, 2H, J = 7.1 Hz, $CO_2CH_2CH_3$), 3.96 (s, 3H, COOMe), 1.47 (t, 3H, J = 7.1 H, $CO_2CH_2CH_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.9, 153.3, 144.6, 135.8, 132.6, 122.1, 120.0, 119.3, 109.2, 107.5, 68.6, 52.2, 14.5. MS (CI): *m/z*: 309 [*M*+1]. IR (KBr, cm^{-1}): ν = 2955, 1799, 1710, 1524, 1452, 1373, 1343, 1239, 1208, 1096, 1013, 953, 808, 743, 624 cm^{-1}. Elemental analyses for $C_{13}H_{12}N_2O_7$: calcd (%) C 50.65, H 3.92, N 9.09 found (%) C 50.49, H 3.98, N 9.11.

*Methyl 5-nitro-1-(tosyloxy)-1H-indole-3-carboxylate (**6b**)*

Reaction time: 6 h. Flash chromatography (Hexane: EtOAc =70:30). Yellow plate, m.p. 145-147 °C, yield = 57%, (223 mg, 0.57 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.02 (d, 1H, J = 2.2 Hz, H4), 8.03 (dd, 1H, ^{3}J = 9.1 Hz, ^{4}J = 2.2 Hz, H6), 7.83 (s, 1H, H2), 7.75 (d, 2H, J = 8.3 Hz, H2' + H6'), 7.38 (d, 2H, J = 8.3 Hz, H3' + H5'), 7.05 (d, 1H, J = 9.1 Hz, H7), 3.96 (s, 3H, COOMe), 2.49 (s, 3H, $SO_2C_6H_4Me$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.7, 148.8, 144.5, 136.3, 133.2, 131.1, 129.9, 129.2, 122.0, 119.9, 119.1, 109.9, 108.1, 52.3, 22.4. MS (CI): *m/z*: 391 [*M*+1]. IR (KBr, cm^{-1}): ν = 2955, 2924, 2853, 1716, 1623, 1594, 1529, 1444, 1402, 1344, 1197, 1181, 1090, 1013, 815, 744, 693 cm^{-1}. Elemental analyses for $C_{17}H_{14}N_2O_7S$: calcd (%) C 52.31, H 3.61, N 7.18 found (%) C 52.45, H 3.75, N 7.21.

*Methyl 1-(benzyloxycarbonyloxy)-5-nitro-1H-indole-3-carboxylate (**6c**)*

Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =80:20). Yellow oil, yield = 60%, (223 mg, 0.60 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.86 (d, 1H, J = 2.2 Hz, H4), 8.81 (s, 1H, H2), 8.20 (dd, 1H, ^{3}J = 8.7 Hz, ^{4}J = 2.2 Hz, H6), 7.80 (d, 1H, J = 8.7 Hz, H7), 7.53 – 7.42 (m, 5H, CH_2Ph), 5.46 (s, 2H, CH_2Ph), 3.89 (s, 3H, COOMe). ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 163.9, 153.2, 144.3, 136.0, 135.0, 134.6, 129.9, 129.6, 128.8, 127.3, 122.0, 120.1, 118.1, 111.0, 73.5, 52.4. MS (CI): *m/z*: 371 [*M*+1]. IR (film, cm^{-1}): ν = 2953, 1803, 1714, 1524, 1452, 1376, 1340, 1234, 1205, 1096, 1020, 959, 806 cm^{-1}. Elemental analyses for $C_{18}H_{14}N_2O_7$: calcd (%) C 58.38, H 3.81, N 7.56 found (%) C 58.51, H 3.90, N 7.63.

*Methyl 5-cyano-1-methoxy-1H-indole-3-carboxylate (**6d**)*

Reaction time: 7 h. Flash chromatography (Hexane- EtOAc =70:30). Yellow oil, yield = 43%, (99 mg, 0.43 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.73 (s, 1H, H2), 8.42 (d, 1H, J = 1.0 Hz, H4), 7.79 (d, 1H, J = 8.5 Hz, H7), 7.71 (dd, 1H, ^{3}J = 8.5 Hz, ^{4}J = 1.0 Hz, H6), 4.19 (s, 3H, N-OMe), 3.86 (s, 3H, COOMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.4, 133.8, 130.7, 128.0, 126.8, 122.6, 120.2, 110.1, 106.3, 105.1, 67.6 , 51.9. MS (CI): *m/z*: 231 [*M*+1]. IR (film, cm^{-1}): ν = 2954, 2850, 2229, 1769, 1707, 1601, 1523, 1454, 1372, 1242, 1212, 1123, 1096, 1021, 988, 803, 766, 689 cm^{-1}. Elemental analyses for $C_{12}H_{10}N_2O_3$: calcd (%) C 62.60, H 4.38, N 12.17 found (%) C 62.77, H 4.43, N 12.31.

*Methyl 5-cyano-1-(phenylcarbonyloxy)-1H-indole-3-carboxylate (**6e**)*

Reaction time: 8 h. Flash chromatography (Hexane-EtOAc =80:20). Colourless prism, m.p. 173-175 °C, yield = 56%, (180 mg, 0.56 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, 1H, J = 1.2 Hz, H4), 8.24 (dd, 2H, ^{3}J = 7.5 Hz, ^{4}J = 1.4 Hz, H2' + H6'), 8.07 (s, 1H, H2), 7.80 (tt, 1H, ^{3}J = 7.5 Hz, ^{4}J = 1.4 Hz, H4'), 7.63 (tt, 2H, ^{3}J = 7.5 Hz, ^{4}J = 1.4 Hz, H3' + H5'), 7.55 (dd, 1H, ^{3}J = 8.6 Hz, ^{4}J = 1.2 Hz, H6), 7.38 (d, 1H, J = 8.6 Hz, H7), 3.97 (s, 3H, COOMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.2, 164.1, 135.9, 135.2, 132.4, 130.9, 129.7, 127.9, 127.3, 125.2, 122.8,

120.0, 110.0, 106.7, 106.2, 52.0. MS (CI): *m/z*: 321 [*M*+1]. IR (KBr, cm^{-1}): ν = 2917, 2849, 2224, 1774, 1709, 1600, 1528, 1452, 1369, 1236, 1216, 1123, 1086, 1022, 989, 805, 767, 699 cm^{-1}. Elemental analyses for $C_{18}H_{12}N_2O_4$: calcd (%) C 67.50, H 3.78, N 8.75 found (%) C 67.43, H 3.87, N 8.66.

*6-Methyl-7-H-7-methoxy-10-Nitro-Indolo[2,3-c]quinoline (**7**)*

To a stirred solution of *N*-(2-(1-methoxy-5-nitro-1*H*-indol-3-yl)phenyl)ethanamide **3e** (70 mg, 0.22 mmol) in acetonitrile (15 mL), $POCl_3$ (30 µL, 0.32 mmol) was added and the mixture was heated at reflux for 8 h. At reaction complete, the mixture was cooled to 0 °C, then poured into water and aqueous ammonia (28 % solution) was added dropwise until pH = 8 was reached. The aqueous layers were extracted with EtOAc. The organic layers were dried over Na_2SO_4, filtered and rotary evaporated to give 58 mg (0.20 mmol)of an orange solid (prism), yield = 91%, m.p. 214°C.

^{1}H-NMR (400 MHz, DMSO-d_6): δ = 9.55 (d, 1H, J = 2.0 Hz, H11), 8.91 (d, 1H, J = 7.9 Hz, H4), 8.58 (dd, 1H, ^{3}J = 8.3 Hz, ^{4}J = 2.0 Hz, H9), 8.25 (d, 1H, J = 7.9 Hz, H1), 8.12 (d, 1H, ^{3}J = 8.3 Hz, H8), 7.88 (m, 2H, H2 + H3), 4.33 (s, 3H, N-OMe), 3.20 (s, 3H, Me). ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 145.7, 143.2, 142.6, 138.6, 130.1, 129.8, 128.0, 127.4, 123.6, 122.9, 122.6, 120.3, 117.9, 117.0, 110.6, 67.2, 22.5. MS (CI): *m/z*: 308 [*M*+1]. IR (KBr, cm^{-1}): ν = 2923, 2361, 1583, 1511, 1461, 1335, 1073 cm^{-1}. Elemental analyses for $C_{17}H_{13}N_3O_3$: calcd (%) C 66.44, H 4.26, N 13.67 found (%) C 66.38, H 4.35, N 13.75.

*Methyl 1-hydroxy-3-phenyl-1H-indole-7-carboxylate (**8a**)*

Reaction time: 9 h. Flash chromatography (CH_2Cl_2-hexane=70:30 Rf = 0.38). Yellow prism, m.p. 99-101 °C yield = 64%, (171 mg, 0.64 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 12.27 (s, 1H, N-OH), 8.17 (d, 1H, J = 7.8 Hz, H6), 7.99 (d, 1H, J = 7.8 Hz, H4), 7.64 (d, 2H, J = 7.6 Hz, H2' + H6'), 7.52 (s, 1H, H2), 7.50 (t, 2H, J = 7.6 Hz, H3' + H5'), 7.36 (t, 1H, J = 7.8 Hz, H4), 7.16 (t, 1H, J = 7.6 Hz, H4'), 4.07 (s, 3H, COOMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.7, 134.7, 130.6, 129.3, 128.3, 127.4, 127.3, 126.8, 124.9, 122.7, 119.2, 114.1, 112.2, 53.7. MS (CI): *m/z*: 268 [*M*+1]. IR (KBr, cm^{-1}): ν = 3118, 3007, 2957, 2858, 2788, 1718, 1662, 1600, 1525, 1442, 1381, 1269, 1203, 1143, 1069, 993, 879, 752 cm^{-1}. Elemental analyses for $C_{16}H_{13}NO_3$: calcd (%) C 71.90, H 4.90, N 5.24 found (%) C 72.03 H 4.87, N 5.41.

*Methyl 1-benzoyl-7-phenyl-7,7a-dihydro-1H-azirino[1,2-a]indole-7-carboxylate (**9a**)*

Reaction time: 5 h. Flash chromatography (CH_2Cl_2- EtOAc =95:5 Rf = 0.28). Orange prism, m.p. 134-136 °C yield = 57%, (211 mg, 0.57 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, 1H, J = 7.8 Hz, H6), 7.51 (d, 1H, J = 7.6 Hz, H3), 7.44 (t, 1H, J = 7.6 Hz, H5), 7.31-7.25 (m, 4H, H4 + H2'' + H6'' + H4''), 7.10 (t, 2H, J = 7.7 Hz, H3'' + H5''), 7.06 (d, 2H, J = 7.7 Hz, H2' + H6'), 6.89 (t, 2H, J = 7.6 Hz, H3' + H5'), 6.75 (t, 1H, J = 7.4 Hz, H4'), 4.63 (d, 1H, J = 7.0 Hz, H1 aziridine ring), 3.71 (s, 3H, COOMe), 3.67 (d, 1H, J = 7.0 Hz, H7a aziridine ring). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.9, 173.4, 154.1, 137.4, 136.6, 134.4, 132.9, 129.4, 128.8, 128.1, 128.0, 127.8, 127.7, 127.3, 125.3, 122.6, 68.0, 54.9, 53.6, 50.2. MS (CI): *m/z*: 370 [*M*+1]. X-ray characterization of compound **9a** was previously reported.[30] IR (KBr, cm^{-1}): ν = 3077, 2953, 2849, 1959, 1732, 1687, 1598, 1469, 1450, 1220, 1021, 956, 734 cm^{-1}. Elemental analyses for $C_{24}H_{19}NO_3$: calcd (%) C 78.03, H 3.79, N 12.99 found C 78.15, H 3.87, N 12.81.

*Methyl 1-(4-nitrobenzoyl)-7-(4-nitrophenyl)-7,7a-dihydro-1H-azirino[1,2-a]indole-7-carboxylate (**9b**)*

Reaction time: 6 h. Flash chromatography (CH_2Cl_2- EtOAc =95:5 Rf = 0.22). Orange leaflet, m.p. 108-110 °C, yield = 60%, (276 mg, 0.47 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, 2H, J = 8.7 Hz, H3'' + H5''), 7.81 (d, 2H, J = 8.7 Hz, H3' + H5'), 7.56-7.49 (m, 4H, H2'' + H6'' + H6 + H3), 7.44 (t, 1H, J = 7.3 Hz, H5), 7.30-7.34 (m,

3H, H2' + H6' + H4), 4.68 (d, 1H, J = 6.7 Hz, H1 aziridine ring), 3.77 (d, 1H, J = 6.7 Hz, H7a aziridine ring), 3.75 (s, 3H, COOMe). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 190.9, 172.0, 167.4, 153.0, 150.4, 147.3, 145.0, 140.3, 133.5, 130.2, 128.8, 128.5, 127.6, 126.2, 124.0, 123.6, 122.9, 54.7, 54.1, 49.5. MS (CI): *m/z*: 460 [*M*+1]. IR (KBr, cm^{-1}): ν = 2956, 2924, 2853, 1935, 1735, 1695, 1604, 1525, 1350, 1241, 1209, 1108, 854, 737 cm^{-1}. Elemental analyses for $C_{24}H_{17}N_3O_7$: calcd (%) C 62.75, H 3.73, N 9.15 found C 62.65, H 3.87, N 9.24.

*Methyl 1-(4-cyanobenzoyl)-7-(4-cyanophenyl)-7,7a-dihydro-1H-azirino[1,2-a]indole-7-carboxylate(**9c**)*
Reaction time: 5 h. Flash chromatography (Hexane- EtOAc =70:30, Rf = 0.28). Light brown oil, yield = 48%, (202 mg, 0.48 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, 2H, J = 8.2 Hz, H3'' + H5''), 7.76 (d, 2H, J = 7.8 Hz, H3' + H5'), 7.64 (d, 2H, J = 8.2 Hz, H2'' + H6''), 7.60 (d, 1H, J = 7.5 Hz, H6), 7.43 (d, 2H, 7.8 Hz, H2' + H6'), 7.35 (d, 1H, J = 7.5 Hz, H3), 7.15 (t, 1H, J = 7.5 Hz, H5), 7.07 (t, 1H, J = 7.5 Hz, H4), 4.65 (d, 1H, J = 6.6 Hz, H1 aziridine ring), 3.73 (s, 3H, COOMe), 3.68 (d, 1H, J = 6.6 Hz, H7a aziridine ring). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 191.3, 171.2, 148.9, 147.5, 139.5, 137.8, 132.5, 132.2, 129.7, 128.8, 127.1, 127.0, 126.7, 125.6, 118.2, 117.7, 117.0, 116.5, 65.8, 54.3, 54.2, 49.5. MS (CI): *m/z*: 420 [*M*+1]. IR (film, cm^{-1}): ν = 3064, 2961, 2928, 2229, 1730, 1693, 1605, 1502, 1263, 1177, 1019, 840, 736 cm^{-1}. Elemental analyses for $C_{26}H_{17}N_3O_3$: calcd (%) C 74.45, H 4.09, N 10.02 found (%) C 74.57, H 4.01, N 10.21.

*Methyl 1-(4-chlorobenzoyl)-7-(4-chlorophenyl)-7,7a-dihydro-1H-azirino[1,2-a]indole-7-carboxylate (**9d**)*
Reaction time: 7 h. Flash chromatography (Hexane- EtOAc =70:30, Rf = 0.34). Orange oil, yield = 56%, (246 mg, 0.56 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, 1H, J = 7.8 Hz, H6), 7.47-7.42 (m, 2H, H5 + H3), 7.29 (m, 1H, H4), 7.25 (d, 2H, J = 8.6 Hz, H2'' + H6''), 7.14 (d, 2H, J = 8.6 Hz, H3'' + H5''), 6.95 (d, 2H, J = 8.6 Hz, H2' + H6'), 6.85 (d, 2H, J = 8.6 Hz, H3' + H5'), 4.58 (d, 1H, J = 7.0 Hz, H1 aziridine ring), 3.71 (s, 3H, COOMe), 3.65 (d, 1H, J = 7.0 Hz, H7a aziridine ring). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 190.9, 172.5, 153.4, 139.6, 136.0, 134.1, 133.7, 133.5, 129.9, 129.3, 128.7, 128.6, 128.3, 128.2, 127.4, 122.4, 61.9, 54.4, 53.3, 49.6. MS (CI): *m/z*: 440 / 438 [*M*+1 (^{37}Cl/^{35}Cl)]. IR (film, cm^{-1}): ν = 2953, 2925, 2853, 1732, 1687, 1589, 1491, 1237, 1093, 1015, 959, 733 cm^{-1}. Elemental analyses for $C_{24}H_{17}Cl_2NO_3$: calcd (%) C 65.77, H 3.91, N 3.20 found (%) C 65.61, H 3.76, N 3.17.

*Methyl 1-(4-methoxybenzoyl)-7-(4-methoxyphenyl)-7,7a-dihydro-1H-azirino[1,2-a]indole-7-carboxylate (**9e**)*
Reaction time: 4 h. Flash chromatography (Hexane-EtOAc =50:50, Rf = 0.30). Light brown oil, yield = 64%, (275 mg, 0.64 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, 1H, J = 7.6 Hz, H6), 7.47 (d, 1H, J = 7.6 Hz, H3), 7.42 (t, 1H, J = 7.6 Hz, H5), 7.30 (d, 2H, J = 8.4 Hz, H2'' + H6''), 7.24 (t, 1H, J = 7.6 Hz, H4), 6.92 (d, 2H, J = 8.5 Hz, H2' + H6'), 6.59 (d, 2H, J = 8.4 Hz, H3'' + H5''), 6.38 (d, 2H, J = 8.5 Hz, H3' + H5'), 4.55 (d, 1H, J = 6.8 Hz, H1 aziridine ring), 3.80 (s, 3H, COOMe), 3.71 (s, 3H, OMe), 3.63 (d, 1H, J = 6.8 Hz, H7a aziridine ring), 3.51 (s, 3H, OMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 190.9, 172.4, 168.2, 164.0, 158.9, 141.7, 141.6, 137.1, 131.4, 131.1, 130.9, 129.5, 128.9, 126.7, 114.5, 114.4, 113.6, 113.5, 65.8, 56.7, 55.5, 55.3, 54.9, 49.1. MS (CI): *m/z*: 430 [*M*+1]. IR (film, cm^{-1}): ν = 2959, 2852, 1731, 1676, 1600, 1512, 1299, 1257, 1176, 1029, 801, 733 cm^{-1}. Elemental analyses for $C_{26}H_{23}NO_5$: calcd (%) C 72.71, H 5.40, N 3.26 found (%) C 72.55, H 5.48, N 3.32.

cis-Dimethyl (1R,7R*,7aR*)-1-benzoyl-7-phenyl-7,7a-dihydro-1H-azirino[1,2-a]indole-4,7-dicarboxylate (**9f**)*
Reaction time: 8 h. Flash chromatography (Hexane- EtOAc =70:30, Rf = 0.22). Colourless prism, m.p. 147-149 °C, yield = 32%, (90 mg, 0.32 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, 1H, J = 1.2 Hz, H3), 7.97 (dd, 1H, ^{3}J = 8.0 Hz, ^{4}J = 1.2 Hz, H5), 7.58 (d, 1H, J = 8.0 Hz, H6), 7.32 (m, 3H, H2'' + H4'' + H6''), 7.11 (t, 2H, J = 7.6 Hz, H3'' + H5''), 7.03 (d, 1H, J = 7.6 Hz, H2' + H6'), 6.90 (t, 2H, J = 7.6 Hz, H3' + H5'), 6.77 (t, 1H, J = 7.6 Hz, H4'),

4.67 (d, 1H, J = 7.1 Hz, H1 aziridine ring), 3.97 (s, 3H, COOMe), 3.72 (s, 3H, COOMe), 3.71 (d, 1H, J = 7.1 Hz, H7a aziridine ring). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 192.3, 172.4, 166.7, 154.1, 139.1, 136.7, 136.0, 132.7, 131.3, 128.5, 128.4, 127.8, 127.5, 127.3, 126.7, 126.4, 123.3, 62.2, 54.8, 53.4, 52.2, 49.8. MS (CI): *m/z*: 428 [*M*+1]. IR (film, cm^{-1}): ν = 2951, 2928, 2856, 2257, 1753, 1722, 1689, 1596, 1580, 1435, 1289, 1250, 1222, 907, 733 cm^{-1}. Elemental analyses for $C_{26}H_{21}NO_5$: calcd (%) C 73.06, H 4.95, N 3.28 found (%) 72.87, H 4.77, N 3.43.

*trans-Dimethyl 1-benzoyl-7-phenyl-7,7a-dihydro-1H-azirino[1,2-a]indole-4,7-dicarboxylate (**9g**)*
Reaction time: 8 h. Flash chromatography (Hexane- EtOAc =70:30, Rf = 0.30). Orange-brown oil, yield = 21%, (137 mg, 0.21 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, 2H, J = 7.6 Hz, H2'' + H6''), 7.80 (dd, 1H, ^{3}J = 8.1 Hz, ^{4}J = 1.2 Hz, H5), 7.74 (d, 1H, J = 1.2 Hz, H3), 7.68 (d, 1H, ^{3}J = 8.1 Hz, H6), 7.58 (t, 1H, J = 7.6 Hz, H4''), 7.46 (t, 2H, J = 7.6 Hz, H3'' + H5''), 7.37 – 7.28 (m, 5H, H2'-H3'-H4'-H5'-H6'), 4.02 (d, 1H, J = 5.2 Hz, H1 aziridine ring), 3.88 (s, 3H, COOMe), 3.82 (s, 3H, , COOMe), 3.79 (d, 1H, J = 5.2 Hz, H7a aziridine ring). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 192.5, 171.5, 166.4, 149.5, 144.8, 142.3, 137.0, 133.8, 130.4, 129.1, 128.7, 128.4, 127.9, 127.7, 126.7, 126.1, 122.1, 62.2, 55.3, 52.6, 52.2, 47.8. MS (CI): *m/z*: 428 [*M*+1]. IR (film, cm^{-1}): ν = 2952, 2926, 2854, 2257, 1761, 1723, 1685, 1597, 1580, 1436, 1289, 1248, 1223, 909, 732 cm^{-1}. Elemental analyses for $C_{26}H_{21}NO_5$: calcd (%) C 73.06, H 4.95, N 3.28 found (%) C 72.98 H 4.87, N 3.31.

*Dimethyl 1-(4-nitrobenzoyl)-7-(4-nitrophenyl)-7,7a-dihydro-1H-azirino[1,2-a]indole-4,7-dicarboxylate (**9h**)*
Reaction time: 6 h. Flash chromatography (Hexane-EtOAc =50:50, Rf = 0.26). Light orange oil, yield = 44%, (228 mg, 0.44 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, 1H, J = 1.5 Hz, H3), 8.03 (d, 2H, J = 8.7 Hz, H3'' + H5''), 8.02 (dd, 1H, ^{3}J = 8.0 Hz, ^{4}J = 1.5 Hz, H5), 7.82 (d, 2H, J = 8.8 Hz, H3' + H5'), 7.60 (d, 1H, J = 8.0 Hz, H6), 7.53 (d, 2H, J = 8.7 Hz, H2'' + H6''), 7.31 (d, 2H, J = 8.8 Hz, H2' + H6'), 4.73 (d, 1H, J = 6.7 Hz, H1 aziridine ring), 3.98 (s, 3H, COOMe), 3.82 (d, 1H, J = 6.7 Hz, H7a aziridine ring), 3.76 (s, 3H, COOMe). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 190.4, 171.0, 166.2, 153.1, 150.1, 146.9, 143.9, 139.8, 138.0, 132.0, 128.4, 128.0, 127.1, 127.1, 123.7, 123.5, 123.3, 59.5, 54.7, 53.9, 52.4, 49.1. MS (CI): *m/z*: 518 [*M*+1]. IR (film, cm^{-1}): ν = 2924, 2854, 2360, 1757, 1723, 1690, 1524, 1494, 1437, 1349, 1291, 1248, 854, 756 cm^{-1}. Elemental analyses for $C_{26}H_{19}N_3O_9$: calcd (%) C 60.35, H 3.70, N 8.12 found (%) C 60.48, H 3.82, N 8.00.

*2-Bromo-5-nitro-3-phenyl-1*H*-indole (**11a**).*
Reaction time: 5 h. Flash chromatography (CH_2Cl_2-Hexane=70:30). Yellow platelet, m.p. 180-182 °C, yield = 45%, (193 mg, 0.45 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, 1H, J = 1.9 Hz, H4), 8.59 (s, 1H, NH), 8.18 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 1.9 Hz, H6), 7.63 (d, 2H, J = 7.4 Hz, H2' + H6'), 7.56 (t, 2H, J = 7.4 Hz, H3' + H5'), 7.46 (t, 1H, J = 7.4 Hz, H4'), 7.43 (d, 1H, J = 9.0 Hz, H7). ^{13}C-NMR (CDCl3, 100 MHz): δ = 143.1, 139.2, 132.1, 129.7, 129.3, 128.2, 127.2, 119.9, 118.8, 116.7, 111.0, 110.8. MS (CI): *m/z*: 320/318 [*M*+1]. IR (KBr, cm^{-1}): ν = 3382, 2920, 2851, 1711, 1517, 1466, 1330, 1072, 810, 699 cm^{-1}. Elemental analyses for $C_{14}H_9BrN_2O_2$: calcd (%) C 53.02, H 2.86, N 8.83 found (%) C 53.11, H 2.92, N 8.67.

*2-Bromo-3-phenyl-1*H*-indole (**11b**).*
Reaction time: 7 h. Flash chromatography (CH_2Cl_2-Hexane=70:30). Yellow needles, m.p. 102-104 °C, yield = 51%, (140 mg, 0.51 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.23 (s, 1H, NH), 7.70 (d, 1H, J = 7.7 Hz, H4), 7.66 (d, 2H, J = 7.5 Hz, H2' + H6'), 7.51 (t, 2H, J = 7.5 Hz, H3' + H5'), 7.41 – 7.37 (m, 2H, H4' + H7), 7.25 (t, 1H, J = 7.7 Hz, H6), 7.17 (t, 1H, J = 7.7 Hz, H5). ^{13}C-NMR (CDCl3, 100 MHz): δ = 136.6, 133.9, 129.9, 129.0, 127.7,

127.3, 123.2, 121.2, 119.5, 117.5, 111.0, 108.0. MS (CI): *m/z*: 275/273 [*M*+1], IR (KBr, cm^{-1}): ν = 3378, 3059, 2924, 2853, 1710, 1601, 1523, 1473, 1445, 1327, 1264, 743, 699 cm^{-1}. Elemental analyses for $C_{14}H_{10}BrN$: calcd (%) C 61.79, H 3.70, N 5.15 found (%) C 61.92, H 3.55, N 5.06.

Compounds **12b** and **12c** were characterized and spectra and analyses are in agreement with data previously reported in literature.[40]

*5-nitro-3-tosyl-1*H-*indole (**14**)*

Reaction time: 5 h. Flash chromatography (hexane-ethyl acetate = 6:4). Light brown plate, m.p. 204-206 °C (dec.), yield 31%, (98 mg, 0.31 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.45 (s, 1H, NH), 8.84 (d, 1H, ^4J = 2.2 Hz, H4), 8.18 (dd, 1H, ^3J = 9.0 Hz, ^4J = 2.2 Hz, H6), 8.05 (d, 1H, ^3J = 3.0 Hz, H2), 7.94 (d, 2H, *J* = 8.3 Hz, H2' + H6'), 7.50 (d, 1H, *J* = 9.0 Hz, H7), 7.32 (d, 2H, *J* = 8.3 Hz, H3' + H5'), 2.40 (s, 3H, $SO_2C_6H_4$Me). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 148.6, 144.2, 143.7, 139.3, 139.0, 132.4, 130.0, 127.0, 122.7, 119.5, 116.7, 112.5, 21.5 ppm. MS (CI): m/z: 317. IR (KBr, cm^{-1}): ν = 3346, 2961, 2924, 2854, 1593, 1527, 1466, 1419, 1339, 1261, 1143, 1093, 1020, 800 cm^{-1}. Elemental Analysis for $C_{15}H_{12}N_2O_4S$: calcd (%) C, 56.95; H, 3.82; N, 8.86 found (%) C 56.61, H 3.97, N 8.88.

*5-nitro-1,3-ditosyl-1*H-*indole (**15**)*

Reaction time: 5 h. Flash chromatography (hexane-CH_2Cl_2= 30:70). Colourless prism, m.p. 239-240 °C, yield = 25%, (118 mg, 0.25 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.75 (d, 1H, ^4J = 1.9 Hz, H4), 8.43 (s, 1H, H2), 8.28 (dd, 1H, ^3J = 9.2 Hz, ^4J = 1.9 Hz, H6), 8.08 (d, 1H, *J* = 9.2 Hz, H7), 7.95 (d, 2H, *J* = 8.2 Hz, H2' + H6'), 7.87 (d, 2H, *J* = 8.2 Hz, H2'' + H6''), 7.37 (d, 4H, *J* = 8.2 Hz, H3' + H5' and H3'' + H5''), 2.43 (s, 6H, $SO_2C_6H_4$Me). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 147.6, 145.5, 145.4, 138.3, 137.9, 133.9, 133.4, 131.1, 130.7, 130.1, 127.8, 125.6, 124.7, 121.6, 117.3, 114.6, 22.2, 22.0 ppm. MS (CI): *m/z*: 471 [*M*+1]. IR (KBr, cm^{-1}): ν = 2923, 2852, 2362, 1596, 1525, 1346, 1261, 1150, 1086, 812 cm^{-1}. Elemental analyses for $C_{22}H_{18}N_2O_6S_2$: calcd (%) C 56.16, H 3.86, N 5.95 found (%) C 56.25, H 3.92, N 5.81.

Compound 16a and ***compound 16b*** show the same spectroscopic data reported in literature.[43]

*5-Nitro-3-(pyridin-2-yl)-1H-indole (**18a**)*

Reaction time: 5 h. Flash chromatography (CH_2Cl_2- EtOAc =70:30). Orange oil, yield = 39%, (93 mg, 0.39 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.41 (d, 1H, ^{4}J = 2.0 Hz, H4), 8.93 (s, 1H, NH), 8.75 (d, 1H, J = 4.6 Hz, H6'), 8.20 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.0 Hz, H6), 7.92 (d, 1H, J = 2.2 Hz, H2), 7.78 (t, 1H, J = 7.7 Hz, H4'), 7.72 (d, 1H, J = 7.7 Hz, H3'), 7.49 (d, 1H, J = 9.0 Hz, H7), 7.22 (t, 1H, J = 6.5 Hz, H5'). ^{1}H-NMR (400 MHz, DMSO-d_6): δ =12.33 (br, s, 1H, NH), 9.40 (d, 1H, J = 2.3 Hz, H4), 8.70 (d, 1H, J = 4.2 Hz, H3'), 8.42 (d, 1H, J = 2.7, H2), 8.08 (dd, 1H, J^3 = 9.0, J^4 = 2.3 Hz, H6), 8.00 (d, 1H, J = 7.9 Hz, H6'), 7.93 (t, 1H, J = 7 Hz, H5'), 7.65 (d, 1H, J = 9.0 Hz, H7), 7.32 (t, 1H, J = 5.8 Hz, H4'). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 148.6, 147.3, 142.1, 140.5, 138.5, 134.8, 130.4, 124.9, 121.1, 119.2, 117.8, 113.0, 111.5. MS (CI): *m/z*: 240 [*M*+1]. IR(film, cm^{-1}): ν = 3378, 2923, 2330, 1611, 1548, 1505, 1454, 1344, 1320, 1114, 1055, 807, 790 cm^{-1}. Elemental analyses for $C_{13}H_9N_3O_3$: calcd (%) C 61.18, H 3.55, N 16.46 found (%) C 61.39, H 3.64, N 16.61.

*5-Nitro-3-(pyridin-3-yl)-1H-indol-1-ol (**18b**)*

Reaction time: 5 h. Flash chromatography (CH_2Cl_2- EtOAc =50:50). Yellow oil, yield = 46%, (117 mg, 0.46 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 12.24 (s, 1H, N-OH), 8.98 (s, 1H, H2'), 8.76 (d, 1H, J = 2.0 Hz, H4),

8.56 (d, 1H, J = 4.6 Hz, H4'), 8.34 (s, 1H, H2), 8.23 (d, 1H, J = 7.9 Hz, H6'), 8.14 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.0 Hz, H6), 7.68 (d, 1H, J = 9.0 Hz, H7), 7.59 (dd, 1H, ^{3}J = 7.9 Hz, ^{4}J = 4.6 Hz, H5'). ^{13}C-NMR (DMSO-d_6, 100 MHz): δ = 147.8, 147.5, 142.5, 136.8, 135.8, 130.7, 128.7, 125.3, 120.7, 118.4, 117.4, 111.1, 110.6. MS (CI): *m/z*: 256 [*M*+1]. IR(film, cm^{-1}): ν = 3375, 2924, 2331, 1610, 1548, 1503, 1459, 1342, 1319, 1110, 1053, 804, 799 cm^{-1}. Elemental analyses for $C_{13}H_9N_3O_3$: calcd (%) C 61.18, H 3.55, N 16.46 found (%) C 60.99, H 3.47, N 16.15.

*5-Nitro-3-(pyridin-4-yl)-1H-indol-1-ol (**18c**)*
Reaction time: 5 h. Isolated by filtration. Orange-brown plate, m.p. 255-260 (dec.), yield = 57 %, (145 mg, 0.57 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 12.28 (br, 1H, N-OH), 8.86 (d, 1H, J = 2.1 Hz, H4), 8.62 (br, 2H, H3' + H5'), 8.49 (s, 1H, H2), 8.14 (dd, 1H, ^{3}J = 9.0 Hz, ^{4}J = 2.1 Hz, H6), 7.77 (d, 2H, J = 4.9 Hz, H2' + H6'), 7.69 ppm (d, 1H, J = 9.0 Hz, H7). ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 150.6, 142.3, 141.5, 136.7, 129.5, 127.8, 120.2, 118.1, 1161, 111.3, 110.3. MS (CI): *m/z*: 256 [*M*+1]. IR(KBr, cm^{-1}): ν = 3373, 2923, 2331, 1607, 1550, 1505, 1460, 1342, 1316, 1112, 1055, 806, 790 cm^{-1}. Elemental analyses for $C_{13}H_9N_3O_3$: calcd (%) C 61.18, H 3.55, N 16.46 found (%) C 61.01, H 3.62, N 16.27

*(S)-Methyl 2-(tert-butoxycarbonylamino)-3-(4-(5-nitro-1H-indol-3-yl)phenyl)propanoate (**24a**)*
Reaction time: 5 h. Flash chromatography (Hexane-EtOAc =60:40). Yellow prism, m.p. 101-103 °C, yield = 55%, (242 mg, 0.55 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.83 (d, 1H, ^{4}J = 2.2 Hz, H4), 8.76 (s, 1H, NH indole ring), 7.94 (dd, 1H, ^{3}J = 8.8 Hz, ^{4}J = 2.2 Hz, H6), 7.89 (s, 1H, H2), 7.35 (d, 2H, J = 7.5 Hz, H3' and H5'), 7.21 (d, 2H, J = 7.5 Hz, H2' and H6'), 6.92 (d, 1H, J = 8.8 Hz, H7), 5.10 (m, 1H, NH), 4.57 (m, 1H, ArCH$_2$CH), 3.74 (s, 3H, CO$_2$Me), 3.13 (m, 2H, ArCH$_2$CH), 1.42 ppm (s, 9H, CMe$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.4, 157.8, 155.8, 145.8, 137.8, 136.0, 132.8, 130.4, 130.3, 127.6, 126.4, 122.4, 117.5, 97.3, 87.3, 52.8, 38.5, 30.1, 28.7. MS (CI): *m/z*: 440 [*M*+1]. IR (KBr, cm^{-1}): ν = 3368, 2978, 1711, 1616, 1596, 1521, 1468, 1334, 1289, 1166, 1064, 804, 738 cm^{-1}. Elemental analyses for $C_{23}H_{25}N_3O_6$: calcd (%) C 62.86, H 5.73, N 9.56 found (%) C 62.72, H 5.81, N 9.47. $[\alpha]_D^{20}$= +7.81

*(S)-Methyl 3-(4-(5-bromo-1H-indol-3-yl)phenyl)-2-(tert-butoxycarbonylamino)propanoate (**24b**)*
Reaction time: 7 h. Flash chromatography (Hexane-EtOAc =70:30). Pale red prism, m.p. 165-167 °C, yield = 47%, (222 mg, 0.47 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.39 (s, 1H, NH indole ring), 8.04 (s, 1H, H4), 7.55 (d, 2H, J = 8.0 Hz, H3' and H5'), 7.36 – 7.31 (m, 2H, H6 + H7), 7.33 (s, 1H, H2), 7.23 (d, 2H, J = 8.0 Hz, H2' and H6'), 5.06 (m, 1H, NH), 4.66 (m, 1H, C$_6$H$_4$-CH$_2$CH), 3.78 (s, 3H, CO$_2$Me), 3.16 (m, 2H, C$_6$H$_4$-CH$_2$CH), 1.46 ppm (s, 9H, CMe$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.8, 155.5, 135.7, 134.3, 133.9, 130.3, 127.9, 125.7, 123.2, 122.7, 118.1, 114.0, 113.2, 80.4, 88.3, 52.6, 38.5, 30.1, 28.7. MS (CI): *m/z*: 474/472 [*M*+1]. IR (KBr, cm^{-1}): ν = 3313, 2975, 2927, 2853, 1741, 1693, 1504, 1454, 1366, 1165, 1058, 1021, 798, 737 cm^{-1}. Elemental analyses for $C_{23}H_{25}BrN_2O_4$: calcd (%) C 58.36, H 5.32, N 5.92 found (%) C 58.11, H 5.24, N 5.99. $[\alpha]_D^{20}$= +5.18.

*(S)-Methyl 3-(4-(1H-indol-3-yl)phenyl)-2-(tert-butoxycarbonylamino)propanoate (**24c**)*
Reaction time: 8 h. Flash chromatography (Hexane-EtOAc =70:30). Pale yellow prism, m.p. 178-180°C, yield = 50%, (197 mg, 0.50 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.31 (s, 1H, NH indole ring), 7.94 (d, 1H, J = 7.4 Hz, H4), 7.43 (d, 1H, J = 8.4 Hz, H7), 7.32 (d, 2H, J = 8.2 Hz, H3' and H5'), 7.10 (d, 2H, J = 8.2 Hz, H2' and H6'), 7.01 (t, 1H, J = 8.4 Hz, H5), 6.82 (t, 1H, J = 7.4 Hz, H6), 6.70 (s, 1H, H2), 5.05 (m, 1H, NH), 4.56 (m, 1H, C$_6$H$_4$-CH$_2$CH), 3.73 (s, 3H, CO$_2$Me), 3.02 (m, 2H, C$_6$H$_4$-CH$_2$CH), 1.42 ppm (s, 9H, CMe$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 172.6, 155.7, 152.7, 138.8, 136.5, 131.6, 131.2, 130.1, 129.9, 126.7, 125.9, 125.9, 118.3, 97.0, 88.2, 52.7,

38.3, 30.1, 28.7. MS (CI): *m/z*: 395 [*M*+1]. IR (KBr, cm^{-1}): ν = 3364, 2976, 2931, 1712, 1685, 1508, 1440, 1366, 1258, 1166, 1059, 1020, 799, 742 cm^{-1}. Elemental analyses for $C_{23}H_{26}N_2O_4$: calcd (%) C 70.03, H 6.64, N 7.10 found (%) C 70.13, H 6.72, N 7.21. $[\alpha]_D^{20}$=+6.27.

X-ray Structure Determination of 9f, 11a and 15.

Crystals suitable for X-ray analysis were obtained by slow diffusion of hexane into a dichloromethane solution of **9f**, **11a** and **15**.

X-ray Crystallographic Analysis. Well defined single-crystals of species **9f**, **11a** and **15** were chosen for conventional X-ray crystal structure analysis. Diffraction data were collected at rt on a Enraf Nonius CAD4 diffractometer with graphite-monochromatized Mo-Kα radiation (λ = 0.71069 Å). Generator settings: 50 kV, 30 mA). Lorentz-polarization correction and, for **11**, an empirical absorption correction, were applied. The structures was solved by direct methods (SIR92)[62] and expanded using Fourier techniques (SHELX97).[63] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included as riding on their pertinent atoms. The final cycles of full-matrix least-squares refinements were based on F2. All calculations were performed using the WINGX Crystallographic Software Suite.[64] CCDC deposition numbers 948744/948745/948746 for compounds **9f**, **11a** and **15**, respectively. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: þ44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Crystallographic data for **9f**: $C_{26}H_{21}NO_5$, fw = 427.44 g mol^{-1}, colourless prism (crystal size, 0.10 x 0.20 x 0.20 mm^3), monoclinic, $P2_1/a$, a = 11.026(2) Å, b = 16.372(2) Å, c = 12.072(1) Å, β = 104.709(1)°, V = 2107.0(5) $Å^3$, Z = 4, D_{calcd} = 1.347 g cm^{-3} , μ(Mo-Kα) = 0.94 cm^{-1}, scanwidth = (1.00+0.35 tanθ), scanmode = ω-2θ, measured reflections = 3814, observed reflections = 2597, No. of parameters = 289, R1 = 0.0444, wR2 = 0.1131, goodness of fit indicator = 1.011.

Crystallographic data for **11a**: $C_{14}H_9BrN_2O_2$, fw = 317.14 g mol^{-1}, yellow platelet (crystal size, 0.01 x 0.30 x 0.40 mm^3) monoclinic, $P2_1/c$, a = 7.912(3) Å, b = 22.639(4) Å, c = 7.974(4) Å, β = 115.83(3)°, V = 1285.6(8) $Å^3$, Z = 4, D_{calcd} = 1.639 g cm^{-3} , μ(Mo-Kα) = 31.2 cm^{-1}, scanwidth = (1.00+0.35 tanθ), scanmode = ω-2θ, measured reflections = 2332, observed reflections = 1289, No. of parameters = 172, R1 = 0.0470, wR2 = 0.1055, goodness of fit indicator = 1.053.

Crystallographic data for **15**: $C_{22}H_{18}NOS_2 \cdot ½CH_2Cl_2$ fw = 512.97 g mol^{-1}, colourless prism (crystal size, 0.08 x 0.12 x 0.40 mm^3), monoclinic, C2/c, a = 26.322(4) Å, b = 8.101(2) Å, c = 24.287(3) Å, β = 116.20(1)°, V = 4646(1) $Å^3$, Z = 8, D_{calcd} = 1.466 g cm^{-3} , μ(Mo-Kα) = 3.87 cm^{-1}, scanwidth = (0.80+0.35 tanθ), scanmode = ω-2θ, measured reflections = 4210, observed reflections = 2372, No. of parameters = 303, R1 = 0.0704, wR2 = 0.2210, goodness of fit indicator = 1.020.

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